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OF THE

CONGRESS

OF

American Physicians and Surgeons.

TENTH TRIENNIAL SESSION,

HELD AT

WASHINGTON, D. C.

May 9th and 10th, 1916

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MINUTES.

The tenth triennial session of the CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS was held in the Assembly Room of the New Willard Hotel in Washington, D. C., on May 9th and 10th, 1916, according to the programme as ordered by the Executive Committee.

The first meeting was called to order at 2.30 P. M., Tuesday, May 9th, by the President, Dr. William S. Thayer of Baltimore, who announced the subject for discussion to be on "Syphilis," and stated that the first paper would be by Dr. John A. Fordyce of New York. He was followed by Dr. Homer F. Swift of New York and by Dr. Hugh Cabot of Boston. These papers were followed by discussions by Dr. Isadore Dyer of New Orleans, Dr. Hugh T. Patrick of Chicago, Dr. Abner Post of Boston, Dr. William G. Spiller of Philadelphia, Dr. Haven Emerson of New York and Dr. George Walker of Baltimore.

At 8.00 P. M. the Congress assembled in the Assembly Room to listen to the address of the President. The meeting was called to order by the first Vice-President, Dr. Robert G. LeConte of Philadelphia. Dr. Thayer then delivered his address on "Practice and Teaching."

On the following day the meeting was called to order at 3.00 P. M. by the President, Dr. William S. Thayer. The subject to be considered was "Immunization and Its Practical Applications." Papers were read by Dr. Theobald Smith of Princeton, on "The Underlying Problems of Immunization"; by Dr. Ludvig Hektoen of Chicago, on "Vaccine Therapy," and by Dr. William H. Park of New York, on "Serum Therapy." These papers were discussed by Dr. Frank Billings of Chicago, Dr. Rufus I. Cole of New York, Dr. Thomas W. Hastings of New York, Dr. Theodore C. Janeway of Baltimore and Dr. Frederick P. Gay of Berkeley.

Adjournment.

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By Invitation of the Executive Committee.

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Organized June, 1875.

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Dr. George B. Wood,	Philadelphia, Pennsylvania.
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Dr. J. Solis Cohen,	Philadelphia, Pennsylvania.
Dr. De La Sota Y. Lastra,	Seville, Spain.
Dr. George M. Lefferts,	Katonah, New York.
Dr. F. Massei,	Naples, Italy.
Dr. E. J. Moure,	Bordeaux, France.
Dr. Emerich Von Navratil,	Buda-Pest, Hungary.
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Sir Felix Semon,	Bucks, England.
Sir St. Clair Thomson,	London, W., England.

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Dr. Thomas A. De Blois,	Boston, Massachusetts.
Dr. William Lincoln,	Cleveland, Ohio.
Dr. William Porter,	St. Louis, Missouri.
Dr. Beverly Robinson,	New York City.

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Dr. Carl Von Eicken,	Giessen, Germany.
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Dr. Paul Heymann,	Berlin, W., Germany.
Dr. Gustav Killian,	Berlin, W., Germany.
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*Dr. Miles F. Porter,	Fort Wayne, Indiana.
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Dr. Charles F. Stokes,	Philadelphia, Pennsylvania.
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Dr. Wallace I. Terry,	San Francisco, California.
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Dr. Edward W. Walker,	Cincinnati, Ohio.
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Sir William Macewen,	Glasgow, Scotland.
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Prof. Samuel Pozzi,	Paris, France.
Dr. A. W. Mayo Robson,	London, W., England.

Dr. Stephen Smith,	New York City.
Dr. Harold J. Stiles,	Edinburgh, Scotland.
Dr. Alexis Thomson,	Edinburgh, Scotland.
Prof. Dr. F. Trendelenburg,	Leipsic, Germany.

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Organized September, 1883.

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Dr. Rupert Blue,	Washington, D. C.
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Dr. Norman Bridge,	Los Angeles, California.
*Dr. Lawrason Brown,	Saranac Lake, New York.
*Dr. Philip K. Brown,	San Francisco, California.
Dr. Sanger Brown,	Kenilworth, Illinois.
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Dr. George E. Bushnell,	Fort Bayard, New Mexico.
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Dr. Charles F. Collins,	New York City.
Dr. A. Coolidge, Jr.,	Boston, Massachusetts.
*Dr. Bayard T. Crane,	Rutland, Massachusetts.
Dr. John C. Da Costa,	Philadelphia, Pennsylvania.
*Dr. Judson Daland,	Philadelphia, Pennsylvania.

*Dr. Thomas Darlington,	New York City.
Dr. William E. Darnall,	Atlantic City, New Jersey.
Dr. N. S. Davis,	Chicago, Illinois.
Dr. Samuel G. Dixon,	Harrisburg, Pennsylvania.
*Dr. William L. Dunn,	Asheville, North Carolina.
*Dr. Carroll E. Edson,	Denver, Colorado.
Dr. John B. Elliott,	New Orleans, Louisiana.
*Dr. J. H. Elliott,	Toronto, Canada.
*Dr. Livingston Farrand,	Boulder, Colorado.
*Dr. Cleaveland Floyd,	Boston, Massachusetts.
Dr. Willis E. Ford,	Utica, New York.
Dr. Frank T. Fulton,	Providence, Rhode Island.
*Dr. C. Fox Gardiner,	Colorado Springs, Colorado.
Dr. William M. Gibson,	Utica, New York.
Dr. Edward H. Goodman,	Philadelphia, Pennsylvania.
*Dr. Walter A. Griffin,	Sharon, Massachusetts.
*Dr. J. N. Hall,	Denver, Colorado.
Dr. Louis Hamman,	Baltimore, Maryland.
*Dr. I. H. Hance,	Lakewood, New Jersey.
Dr. James A. Hart,	Geneva, New York.
Dr. Thomas W. Hastings,	New York City.
*Dr. Charles J. Hatfield,	Philadelphia, Pennsylvania.
Dr. John B. Hawes, 2nd,	Boston, Massachusetts.
Dr. John L. Heffron,	Syracuse, New York.
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*Dr. Guy Hinsdale,	Hot Springs, Virginia.
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*Dr. G. Walter Holden,	Denver, Colorado.
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*Dr. A. Jacobi,	New York City.
Dr. W. A. Jayne,	Denver, Colorado.
*Dr. Charles G. Jennings,	Detroit, Michigan.
Dr. Collins H. Johnston,	Grand Rapids, Michigan.
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*Dr. Arnold C. Klebs,	Boston, Massachusetts.
Dr. D. Braden Kyle,	Philadelphia, Pennsylvania.
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*Dr. John A. Lichty,	Pittsburgh, Pennsylvania.
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Dr. Thomas J. Mays,	Philadelphia, Pennsylvania.

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Dr. Charles H. Miner,	Wilkes-Barre, Pennsylvania.
Dr. Stanley G. Miner,	Detroit, Michigan.
*Dr. Charles L. Minor,	Asheville, North Carolina.
Dr. James D. Morgan,	Washington, D. C.
Dr. R. C. Newton,	Montclair, New Jersey.
Dr. Estes Nichols,	Portland, Maine.
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*Dr. Robert C. Paterson,	Saranac Lake, New York.
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Dr. Charles E. Quimby,	New York City.
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American Gynecological Society	99	..	31	69
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American Laryngological Association ...	87	24	11	52
American Surgical Association	161	..	17	98
American Climatological and Clinical Association	134	10	15	80
Association of American Physicians	201	..	9	142
American Association of Genito-Urinary Surgeons	65	..	4	39
American Orthopedic Association	94	15	6	72
American Pediatric Society	72	..	7	49
American Association of Pathologists and Bacteriologists	331	..	..	No record
American Society of Tropical Medicine	126	16	32	28
	1908	83	164	927
Total membership of Congress		2155		
Guests and Visitors				111
Total attendance				1038

THE DIAGNOSIS AND GENERAL TREATMENT OF SYPHILIS.

JOHN A. FORDYCE, M.D.

Professor of Dermatology and Syphilology, College of Physicians and Surgeons, Columbia University, New York City.

It cannot be emphasized too frequently nor too emphatically that the fate of the syphilitic individual depends largely upon the early diagnosis of his infection and the intensity with which his treatment is carried out in the first six months. It is in the accomplishment of this purpose that the modern aids to diagnosis have rendered such invaluable service. Unfortunately this is not universally recognized, for clinicians are still met with who decry these modern precision methods, claiming that the trained observer can recognize with his eye and sense of touch all that can be revealed by laboratory procedures. The fallacy of this claim is demonstrated from time to time by patients who come with the following history: 15 to 20 years ago they consulted the best known syphilographer at that time who made a diagnosis of chancroid telling the patient that his future, as far as the present infection was concerned, was secure and that he had nothing to fear. Reassured by such information, no treatment was taken and years after these patients consult for involvement of the central nervous system, an interstitial glossitis, an aortitis, or other late manifestation of the disease. It is now well known that the soft sore frequently harbors the parasite of syphilis, and owing to the longer incubation period of the latter does not develop its characteristic features until after the expiration of two or three weeks or they may be entirely absent. It seems superfluous, therefore, to insist that the secretion of all venereal sores be searched for the treponema pallidum. Failing to find it one should not give a favorable prognosis until repeated examinations have been made including the Wassermann reaction. With proper training the dark field illumination is simple of application and the spirochaete of syphilis readily differentiated from other types. Microscopic corroboration of a suggestive sore is absolutely essential in many cases owing to the protean appear-

ance chancres may assume. While, to the skilled eye and finger, a Hunterian chancre with indurated edges needs no confirmation the pathognomonic features may be lacking altogether, or a papule or herpetic lesion may represent the only local reaction called forth by the treponema. In urethral sores and suspicious extragenital lesions the correct and early diagnosis is of great importance and their nature finds a ready means of differentiation in the dark field. The value of the latter is further appreciated in developing chancres before the clinical characteristics suggestive of the infection appear. Recently I had the opportunity to examine an initial lesion which had made its appearance only on that day. It was situated on the left side of the foreskin, was about the size of a pin head, capped by a tiny crust. The patient had been exposed three weeks before. There was no lymph node enlargement and the Wassermann reaction was negative. The advantage of early treatment in such cases and consequently the more favorable prognosis are too obvious for discussion. Success in demonstrating the organism depends largely on the care taken in obtaining serum for examination. This should be secured from the depths of the lesion. Antiseptic washes, ointments or other applications frequently interfere with the demonstration and in cases of doubt the examination should be repeated on successive days, the lesion being kept clean meanwhile with saline solution.

The time of the appearance of the Wassermann reaction cannot be estimated with mathematical exactness as it is dependent upon the rapidity with which the organisms gain the general circulation and the reaction provoked by them. This we know varies in different individuals. In some cases the reaction is positive in the fourth or fifth week after exposure; in others not until the seventh or eighth week. A negative reaction does not necessarily mean that generalization of the spirochaetae has not taken place. Uhlenhuth and Mulzer[1] obtained positive results in animal inoculations with the blood of primary syphilitics in whom the Wassermann reaction was still negative. With the development of the rash it is usually definitely established. I have in a very long series of untreated cases found only one with a fresh maculo-papular eruption in which the Wassermann was only weakly positive. If treatment is carried out on a definite and intensive plan in the primary stage a negative reaction will remain continuously negative, or in the event of its being already positive it shows itself susceptible of reversion more

readily than where the infection is of several years' duration. Too much stress cannot be laid on the fact that the amount of treatment is individual; this must be kept in view in every case under consideration. There are patients who treated under the old regimé with mercury by mouth, inunctions or injections, or these methods combined, now have a negative blood reaction, exhibit no symptoms referable to the nervous or circulatory system and are negative after a provocative injection of salvarsan. Others treated five years ago with a minimum amount of salvarsan, i. e., one or two injections, and mercury may likewise be considered cured according to our present-day criteria. On the other hand, there are a certain number of patients in whom multiple courses of salvarsan and mercury are necessary to bring about and maintain negative findings. In some cases we will even fail to convert a positive into a negative reaction without endangering the health of the patient. A resistant serum cannot always be accounted for on a clinical basis for often as far as we are able to ascertain nothing can be demonstrated to explain its persistence. In by far the vast majority, however, involvement of the cardio-vascular or nervous system will furnish an explanation.

The interpretation of the Wassermann reaction is as important as that of the clinical phenomena of the disease but the burden of proof should not rest with its presence or absence alone. In ocular syphilis, disease of the vascular apparatus, obscure visceral or nervous involvement, and in latent syphilis of hereditary origin positive manifestations may be present and the Wassermann reaction negative. To make some of these points clear the following cases are quoted:

I. Man, with active secondary skin and throat lesions end of October, 1914. On October 31st, November 8th, 20th, and December 13th, respectively, 0.6 gm. salvarsan. January 8th, 1915, perivasculitis retinae. Wassermann said to have been negative. Under rubbings and calomel eye lesions cleared. Discontinuance of treatment was followed by relapse from a new focus. March 31st, 1915, spinal fluid —; serum —. Under injections of a soluble salt and potassium iodide eye-sight again improved. Treatment interrupted in September; Wassermann December 29th, 1915, —; March 16th, 1916, ++++

II. Man, age 57, with cerebral endarteritis and capillary fibrosis at the maculae. Infection over 30 years ago. Recurring ulcerative

skin lesions; scaling eruption palms; mental depression, vertigo, loss of memory; inability to concentrate on work; failure of sexual power. He recalls severe headaches, leg pains, and mental excitability in secondary period, 29 years ago.

Eye reflexes, knee jerks and ankle jerks present without noticeable abnormality. Treatment during many years with mercury and potassium iodide. Repeated negative Wassermann reactions during 1911 and 1912. In 1913 after treatment with potassium iodide and mercury Wassermann became ++++, and after further treatment —. Spinal fluid March 31st, 1915: Cells 0; globulin ++; Wassermann —; gold test —; blood Wassermann ++++. Treatment continued during 1915 was followed by improvement in all respects. Vertigo and depression disappeared; capacity for work increased. He was less excitable and memory and sexual power returned. Evidence of vascular disease in eye also disappeared.

The noteworthy features in this case are the long persistence of a negative Wassermann reaction with scaling palms, analogous to leukoplakia, the obscure character of the nervous symptoms, evidence of vascular disease in eyes, result of fluid examination pointing to cerebral endarteritis, Wassermann reaction becoming positive after treatment by iodides and mercury, and relief of all symptoms by persistent treatment.

III. Girl, 21 years old, hereditary syphilis. Scars of an old interstitial keratitis. For five years had suffered from migraine type of headache. Serum —; spinal fluid —. After three injections of salvarsan serum became strongly positive.

IV. Man, age 49; chancre when 16 years old followed by secondaries. For three years internal treatment; no relapses. In the summer of 1915 complained of increasing fatigue and soreness over the right apex. Repeated examinations for tubercle bacilli negative. Von Pirquet +, Wassermann —. From X-ray and physical examination diagnosis of syphilis of the bronchial glands was made. Wassermann January 7th, 1916, —; January 11th, 1916, —; mixed treatment for one week evoked a ++++ reaction.

The above abstracts show that not rarely it requires not a single but several injections of salvarsan or the prolonged use of mercury and potassium iodide before a provocative reaction is obtained.

The Wassermann test is of great value in the recognition of syphilis as a causative factor in conditions of obscure etiology in

children. Also in anticipating some future development as in many cases of congenital syphilis no sign or symptom is present excepting a positive blood reaction. The children are normal mentally and physically and excepting the positive serum and a history of syphilis in the father there is nothing suggestive of a luetic taint.

The tendency of the present day is to deny categorically the paternal origin of syphilis admitting only the possibility of transmission from the maternal side. While this would simplify the problem, it offers no solution for the cases where the mothers remain symptom-free and Wassermann negative—some patients observed after 30 years who have had one or more children clinically and serologically syphilitic. Do such women have a modified form which disappears spontaneously or do they escape the infection altogether?

The only criterion of cure in a man contemplating matrimony is a negative Wassermann which has persisted for at least a year after intensive treatment and which remains negative after a provocative salvarsan. The element of time while of importance in modifying the infection is of vastly less value than the revelation of the serological test. In a family seen by me a short time ago the father was infected in 1901, for which he had inunctions and potassium iodide each year for six years. He was married in 1907. The first child was born in 1908, was well-nourished and healthy until August, 1915, when he developed partial deafness of the right ear. His spinal fluid showed cells 20; globulin ++; Wassermann —; serum +++. The second child was born in 1913, is splendidly developed in every way and has never shown any symptoms but has a four plus Wassermann. The mother's reaction is negative; she has never given any evidence of the infection, has had no miscarriages and no treatment. The father's reaction is ++++.

The diagnostic import of the spinal fluid examination grows more and more apparent with time. The cell count, Wassermann reaction, globulin and colloidal gold tests enable us not only to determine the activity of a syphilitic process in the brain or cord but serve to distinguish the various pathological types of syphilis affecting the cerebro-spinal system and in many cases to differentiate between these and non-luetic affections. A case in point is the simulation of the multiple neuritis of diabetes by the tabetic syndrome. A patient, aged 37, was referred to me with the diagnosis

of tabes. He had had a chancre 12 years before, followed by secondaries and treatment for three years. For four weeks he had had pain and numbness in his fingers and feet with an insecure feeling in the soles of his feet, difficulty in walking and unsteadiness; for 6 or 7 years he had had periodic attacks of gastric distress with dizziness and extensive areas of hyperaesthesia; sexual paresis had been present for one year; eyes were normal, patellar and Achilles reflexes absent. Laboratory examination showed blood Wassermann —; spinal fluid: cells 8; globulin —; Wassermann —. His urine contained a large amount of sugar. Diagnosis: diabetic polyneuritis.

Another case was sent with the diagnosis of tabo-paresis. The patient gave a history of syphilis 25 years previously with repeated courses of treatment. His pupils were irregular and fixed to light, knee jerks absent and lightning pains in the lower extremities. It was claimed that he had shown evidence of mental deterioration as manifested by irascibility, loss of memory, etc. The patient had been alcoholic for over 30 years having taken 6 or 8 drinks daily with occasional intermissions. His blood and fluid examinations were absolutely negative. In this case a correct diagnosis might have been made by a skilled diagnostician but to the average practitioner the picture presented was that of tabes or tabo-paresis. From the laboratory standpoint there are two possible conclusions; either the spinal fluid findings were rendered negative by the treatment received or the entire syndrome was due to alcoholism and the question of syphilis as an etiological factor left in doubt. The latter supposition is the more probable, experience having shown that in paresis negative findings throughout are not brought about by the amount of treatment the patient has had.

With faulty diagnoses like the above on the negative side of syphilis, those on the positive side merit citation, for not infrequently patients with obscure pains, febrile attacks, gastric and rectal crises, irritability, failure of memory, etc., give a history of having long been treated for neuraesthenia, rheumatism, neuritis and various other indefinite conditions. Such patients sometimes admit having had a specific infection with indifferent treatment; others disclaim all such knowledge.

One of my clinic patients, a young woman, 24 years old, had had within the past 2 years about 20 attacks of gastric crises. She was usually removed to a hospital and on two occasions was operated

upon, once for appendicitis and again for gall stones. She has been married 5 years and has had several miscarriages. The only objective manifestation of tabes was slightly sluggish pupils. Her serum was strongly positive, her spinal fluid showed 45 cells, ++ globulin, Wassermann ++++ to 0.6; colloidal gold, luetic curve.

Rectal crises are less commonly seen and their nature often fails of recognition. A patient under my care was treated 19 years ago for primary and secondary syphilis. For the past two years he had had attacks of severe pain in the rectum for which an operation had been advised. His pupils were unequal and sluggish to light, knee jerks normal, station good, bladder slow, sexual power weak. Blood ++++, spinal fluid: cells 150; globulin ++; Wassermann ++++ to 0.4; colloidal gold, luetic curve. His pains were markedly aggravated by the first few intraspinal treatments.

The so-called lightning pains in tabetics are often treated symptomatically or disregarded entirely. A patient aged 34, infected 10 years ago, had suffered from pains in his legs for 7 years. His spinal fluid showed cells 42; globulin ++; Wassermann ++++ to 0.2; colloidal gold test, luetic curve; serum ++++. Another patient, 39 years of age, infected 7 years ago, complained chiefly of stabbing pains in various parts of the body which began 4 years ago in the lower extremities. His pupils were irregular and sluggish to light, his knee jerks weak, ankle jerks absent. Spinal fluids: cells 8; globulin ++; Wassermann ++++ to 0.2; colloidal gold test, luetic curve; serum ++++.

The premonitory symptoms of developing paresis are also frequently overlooked. This is illustrated by the following case: Man, 42 years of age, infection in 1905, for which he was treated for 7 years with mercury internally and by injection. He had had no symptoms since 1912. In June, 1915, he had a convulsion, unconsciousness lasting one-half hour. The attack was attributed to colitis and intestinal absorption and treatment directed against this until December, 1915, when he had a second convulsion. His spinal fluid showed cells 45; globulin +++; Wassermann ++++ to 0.1; colloidal gold test, paretic curve; serum ++++.

In the light of more recent investigations an analysis of the spinal fluid is not complete unless the gold sol. test is performed in addition to the Wassermann reaction and cytological and chemical examination. The theory of this reaction is based upon the

observation made by Zsigmondy in his original work on metallic colloidal solutions in 1901 that solutions of electrolytes precipitate colloidal gold; that in the absence of an electrolyte proteins will also cause such a precipitation, while in the presence of an electrolyte they inhibit precipitation. These principles were applied by Lange[2] in 1912 to the examination of the spinal fluid. He found that by a modification of the Zsigmondy technic normal and pathological fluids could be differentiated from each other as well as syphilitic from other affections of the central nervous system. While the test has been employed by a number of workers during the past few years in the diagnosis of syphilis it has not had the general application it deserves owing to the difficulty of making the solution. This phase happily is now in a large measure overcome by the admirable work of Dr. Miller[3] and his associates. Through their investigations every detail in connection with the technic of its preparation has been so carefully developed that the standardization of the reagent is now possible and consequently more uniform results in the reaction.

Just how the reaction occurs and the nature of the protein or proteins involved is not known. Views advanced are that it is due to the presence of abnormal albumin or possibly the presence of an excessive amount of the normal. It was originally found that the colloidal gold was a qualitative determination which according to dilution gave different reactions. Lange therefore sought the explanation in a different qualitative mixture of proteins while Zalozieki interpreted it as an immunity reaction and Jaeger and Goldstein as a physical phenomenon of an electrical nature. Miller, Brush, Hammers and Felton have shown that the substance is dialysable. The amount of albumin normally present in the spinal fluid gives no reaction and a change in reaction is therefore indicative of some abnormality as to quantity or quality.

The test itself, very easily and quickly made, consists of a series of color changes which occur so characteristically and constantly that they may be said to be specific. It is performed with ten dilutions of spinal fluid in geometrical progression from 1-10 to 1-5120. The color change depends on the amount of colloidal gold precipitated and varies from the negative salmon red through red-blue, lilac or blue, blue-gray or gray, and colorless. These changes may be plotted in curves or are arbitrarily expressed from zero to five. A negative colloidal gold would show no change and would

therefore be expressed as 0000000000. In tabes and cerebro-spinal syphilis the reaction occurs in the lower dilutions with the intensity of the change in the third and fourth or fourth and fifth tubes. The term "luetic zone" or "luetic curve" is used to describe this reaction. The reading would be as follows: 1133200000 or 1223320000. In meningitis of non-syphilitic origin the maximum change occurs beyond the syphilitic zone, that is, in the higher dilutions, while in paresis precipitation of the colloidal gold occurs regularly in the first four to eight tubes with decolorization or a turbidity, and the reading represented as 5555-431000 or as many fives as there are decolorized tubes. To this zonal change Miller and Levy applied the term "paretic curve." A properly standardized, that is, a neutral solution of colloidal gold shows either no change at all with a normal spinal fluid or produces a slight variation with a bluish nuance in the first four or five tubes which is negligible. Some cases may even give a change to a frank red-blue in the first four tubes so that the reading would be 1111000000, but with all the other laboratory findings negative it has been shown this has no diagnostic import.

It may be said that as a rule there is a parallelism between the other positive findings in the fluid and a positive gold reaction. The significance of any one of the individual abnormalities must be appreciated before a proper interpretation can be placed upon the laboratory findings. We know that a lymphocytosis alone is not pathognomonic of syphilis as a mild grade is met with in other affections of the central nervous system and that the cell count can not be relied upon to differentiate between tabes, cerebro-spinal syphilis and general paresis as an equally high pleocytosis may be met with in any of these conditions. So too the presence of globulin alone indicates organic disease of the brain or cord but does not separate syphilitic from non-syphilitic disease. More positive information is derived from the complement fixation test as a positive Wassermann occurs only in lues. However, this test by itself does not supply a differential diagnosis as fixation to 0.2 cc. or lower is met with not only in paresis but in some cases of progressive tabes and cerebro-spinal syphilis. On the other hand with a distinctly syphilitic process as in cerebral endarteritis, abortive or stationary forms of tabes and some types of cerebro-spinal syphilis the Wassermann may be completely negative. In the last named cases a supplementary gold test is of value in demonstrating the

luetic nature of the condition. Its greatest value and by far most prominent rôle, however, is in distinguishing between paresis and the conditions which simulate it as well as its prognostic significance in tabetics who show no mental impairment but give a paretic curve. Since the application of the gold sol. test in my laboratory a number of patients in whom no mental involvement was suspected have given the curve characteristic of paresis. The following cases may be cited as illustrations:

Mr. X. Age 39, infection 13 years ago; secondaries denied. Mercury internally for one and one half years. In 1914 he developed pain in his legs, arms and neck. When seen by me in March, 1915, his pupils were fixed to light and accommodation, knee jerks and Achilles jerks were absent; Romberg present, slight bladder incontinence; sexual power weak. Spinal fluid examination: cells 75; globulin ++; Wassermann ++++ to 0.4; colloidal gold, decolorization in first five tubes (5555543200). His family had observed no mental trouble although they thought he had been more irritable and less dependable in business transactions during the preceding year. He has been under active intraspinal treatment; the curve and Wassermann remain unchanged; clinically there has been no change in his condition.

Mr. Y. Age 39, infection in 1897. In 1906 double vision and bladder weakness. In 1912 tingling in feet, unsteadiness in gait and great fatigue. He has absent knee jerks and a Charcot joint of the right hip. The latter part of 1914 according to his family he was depressed and very forgetful. A spinal fluid examination made after he had intensive intravenous and mercurial treatment showed cells 2; globulin ++; Wassermann ++++ to 0.6. A gold sol. test in May, 1915, read 5555432200.

Mr. Z. Age 27. Chancre eight years ago followed by secondaries of the skin and mouth. Treatment internally until 1910 when he developed paralysis of the left external rectus. December 20th, 1912, station and gait normal, knee and ankle jerks hyperactive, coördination perfect, no sensory changes; objectively viscera normal, pupils normal. Complains of shooting pains in legs, tingling and cramps in calves. Blood Wassermann —. Spinal fluid examination in December, 1913; cells 26; globulin +; Wassermann ++++ to 0.4. Colloidal gold test made in May, 1915, and all subsequent ones give a paretic curve. This patient has had since the latter part of 1913, 30 intravenous injections of sal-

varsan and 30 intraspinal injections in addition to mercury. His present fluid examination shows cells 3; globulin +++; Wassermann ++++ to 0.4. He is of powerful physique and during the time he has been under treatment has interrupted his work, which is that of a stationary engineer, only for intraspinal therapy. No change in character or personality has been noted.

In analysing those cases of general paresis which I have had under my care from time to time the striking feature has been the multiform clinical picture and in many the absence of the chief symptoms of the affection; namely, the typical cerebral disorders as writing and speech defects, tremor and memory defects. Some of the patients have had simply a convulsion or two or fainting attacks while a few others have exhibited no signs referable to the condition, the diagnosis being based mainly on the persistent positive Wassermann reaction and the gold sol. test. While it would be premature to make a definite pronouncement as to the prognostic significance of the paretic curve we must bear in mind the teaching of post-mortem findings that anatomical changes in general paresis may long antedate the clinical manifestation. In patients, therefore, who are under continuous observation and especially those who are receiving intraspinal treatment where the fluid can be examined at regular intervals, the presence or the development of the paretic curve should excite a strong suspicion that these patients may later develop the clinical syndrome. My procedure with these patients is to advise the family or business associates of the possibilities in the case, especially where large business interests are involved, and to treat these cases intensively with the hope that we may, perhaps, anticipate, retard or arrest the degenerative cerebral changes. In the type where the meningo-vascular changes are preponderant, as evidenced by a high cell count, the prognosis is more favorable than where the parenchyma is chiefly involved.

The colloidal gold test has been uniformly positive in all cases with the clinical ear-marks of general paresis. In several cases under intensive treatment the paretic curve has changed to the luetic curve. In early syphilis of the central nervous system, i. e., in the early secondary period, I have in several instances found the luetic curve with a negative Wassermann, the only other abnormalities being a slight increase in globulin and lymphocytes. Clinically these cases gave objective evidence of implication of the central nervous system.

In estimating the number of individuals with abnormal spinal fluids in the secondary stage of the infection I have frequently expressed the conviction that no larger percentage showed definite changes than later developed frank symptoms referable to the neural axis. Further experience strengthens this conviction. In a series of cases examined two years ago abnormalities were demonstrated in less than 20%. In a series of 63 cases recently repeated 10 showed very slight changes as to lymphocytosis and globulin content, coming well within the border line cases, while 15 exhibited a definite increase in cells and globulin with a positive Wassermann in 7. The cases were all within the first year of infection, untreated or practically so. The standard used was a cell count over 5, a globulin content demonstrated by the Pandy test, a positive Wassermann with 2.00 cc. or less of fluid and the color changes elicited by the Lange test.

Statistics in the literature treating of abnormal fluids in the secondary stage of lues are variously quoted at from 10 to 90%. In attempting to reconcile such an apparent disparity it is possible that too much significance has been attached to minor changes as increased pressure, increase of a few cells or a trace of globulin. These are probably only transient conditions and part of the systemic infection. My belief is that only such individuals who show very conspicuous changes as evidenced by a definite cell count, globulin and positive Wassermann are candidates for one or the other of the different clinical types of cerebro-spinal syphilis. Whether we invoke special conditions as a particular strain or individual predisposition as necessary corollaries to infection of the central nervous system, the deduction is forced upon us that in a large majority of patients the organisms must be destroyed spontaneously or by therapeutic agents administered in the ordinary way. The proportion of syphilitics who develop disease of the nervous system is given at from 9 to 25%. These figures it must be borne in mind were compiled before the era of laboratory diagnoses and their accuracy cannot pass unchallenged.

Treatment.

In discussing the treatment of syphilis there are certain general considerations in regard to the therapeutic armamentarium worthy of mention. The object of any energetic antiluetic treatment is the destruction of the greatest number of spirochaetae in the shortest

possible time. From our knowledge of the immunological and pathological processes in the disease this is best accomplished in the early stage, and from experience accrued during the past five years is more readily and more certainly brought about by the combination of salvarsan and mercury. It has been amply demonstrated that salvarsan is essentially a spirochaeticide which while it has very little influence on the organisms in the test tube is actively germicidal *in vivo*. Mercury is the best known germicide *in vitro*. When employed experimentally in animals infected with trypanosomiasis or relapsing fever it is practically inert as far as its effect upon the organisms is concerned and the fatal termination of these diseases is not delayed. In spite of this negative evidence, however, it has been demonstrated empirically for many years that mercury has a curative effect in syphilis and since the cure depends upon the more or less complete saturation of the patient with the drug its action is presumably a direct one. Nor has it been shown that the iodides are spirochaetotropic in their action. Potassium iodide has no effect on the early lesions of syphilis and only a negligible one in rendering the Wassermann reaction negative. It has, however, a profound physiological effect aside from its specific therapeutic action. The latter, in gummata, has been explained by Jobling[4] as due to the neutralization of the antiferments which prevent autolysis and absorption of the necrotic tissue, at the same time rendering the infecting organisms which had previously been protected by the necrotic tissue accessible to the parasiticide.

Salvarsan by virtue of its spirochaeticidal properties finds its greatest field of usefulness in primary and secondary syphilis where the organisms are abundant. In the later stages, where they are few in number and the tissue changes are more marked, one would naturally expect less result from this agent. As a matter of fact, in gummatous and periosteal lesions and all the active manifestations of late syphilis the therapeutic effect of the drug is almost as intense as in the early contagious period. This is especially true of patients who have been treated over a long period of years with mercury and potassium iodide and have become more or less immunized to the action of these drugs. I have seen patients with periosteal lesions and febrile attacks and numerous cases of so-called malignant syphilis in whom mercury and potassium iodide were practically inert very quickly respond to salvarsan. The following case is a typical example: Woman; Age 42, infection 11

years ago. Treatment for three years by mouth and injections. When seen September 7th, 1915, she was suffering from periostitis of the right parietal and frontal bones, of the sternum and right shoulder. For several months she had been running an evening temperature of 101 to 101.5 degrees Fahrenheit with headache. During this time mercury and potassium iodide were administered without effect. On September 9th, 1915, she was given 0.25 gm. salvarsan. Her pains, headache and fever disappeared in 2 days and there was a most marked general improvement. Since that time she has had 6 small doses of salvarsan and 2 of neosalvarsan and has gained over 30 pounds in weight.

While it is possible theoretically to formulate a method of treatment in the various stages of syphilis, as a matter of practice the best devised plan must preeminently be an elastic one subject to the modifications called for by the susceptibility of the patient to the drugs and to intercurrent reactions which take place from time to time.

In early active syphilis salvarsan alone has been followed by neuro-recurrences and mono-recurrences or early tertiary lesions. In cases of initial lesion seen before the Wassermann reaction is positive salvarsan may perhaps be given without such danger. It is better, however, not to rely on this drug alone to establish a complete cure but to give the combined treatment. It has been claimed by Wechselman that such combination was more apt to produce kidney involvement but this contention has not been substantiated by the majority of observers. My own plan is to give a course of mercury with the salvarsan, the number and size of doses of both agents depending upon sex, body weight, and general condition of the patient.

The salvarsan is given in courses of 5 to 6 injections in doses of 0.3 gm. to 0.5 gm. for men and 0.25 to 0.4 gm. for women at intervals of one week to ten days. The mercurial injections are given every day or every alternate day if a soluble salt is employed or once a week if an insoluble one. My preference in case of the former is the bichloride of mercury in courses of 20 to 30 injections given daily or every other day. Of the insoluble preparations, grey oil (in the form of mercurial cream), of which 5 minims represents one grain, in series of 10 to 12 injections, or salicylate of mercury (40% suspension) in dosage of one to three grains gradually increased, 10 to 12 injections constituting a course. Both salvar-

san and mercurial courses are followed by a rest period of six weeks and then the procedure is repeated. Wassermann tests are made periodically but treatment is not interrupted in spite of a negative reaction until the adequate amount of medication has been given.

Where visceral lesions are present salvarsan should be used in small doses repeated at intervals determined by each case. In cardiac conditions it is better to precede with mercury or mercury and potassium iodide. They are greatly benefited by the latter drug. I have given salvarsan in these cases without untoward symptoms. Whatever form of treatment is decided upon it is important to carry it out persistently. The progress of any active condition can be checked but anatomical changes like sclerosis or aneurysm are of course permanent.

In primary syphilis before the Wassermann has become positive it is possible to abort the infection both clinically and serologically. While in the past this has been accomplished in some cases with a minimum amount of treatment such patients now receive two courses each of salvarsan and mercurial injections.

In secondary syphilis with a positive Wassermann it is frequently necessary to give three courses of salvarsan with mercury before the desired effect on the serum reaction is obtained.

In tertiary syphilis the method of treatment depends upon the tissues or organs involved. It is of advantage to combine the courses of salvarsan with intramuscular injections of mercury and to follow this with the prolonged use of potassium iodide and mercury in the form of mixed treatment.

In so-called latent syphilis the administration of salvarsan alone often fails. I have a number of cases in whom the Wassermann reaction continued to show complete inhibition after repeated courses. In many individuals with a positive serum where the nervous system is not involved careful examination may reveal an aortitis, interstitial glossitis, or the remains of a hepatitis or other visceral lesion with residua sufficient to call forth a Wassermann reaction. It often requires the most painstaking care to reveal the possible location of the disease. For instance, the nervous system may be implicated and only manifested by slight pupillary irregularity or a slight change in the knee jerks which might easily be overlooked unless the examination is made by a carefully trained clinician. The spinal fluid should be examined where these deviations are indicative of involvement of the cerebro-spinal system and

in all cases with a persistent blood reaction where a focus cannot be determined in the skin, mucous membranes or viscera. Even in the absence of signs pointing to such implication a Wassermann which does not respond to therapy is an indication for lumbar puncture. More benefit is derived in latent lues from the old-fashioned mixed treatment, that is, a combination of mercury and potassium iodide in a liquid menstruum, than from salvarsan alone or combined simply with potassium iodide. With mixed treatment I have in many instances accomplished the reversal of the Wassermann which had remained persistently positive under salvarsan and mercury.

From Stühmer's[5] experiments the greater part of salvarsan introduced intravenously is stored in the lungs, liver and spleen in about equal quantities. These form depots from which the drug reaches the circulation, most of it probably passing unchanged through the kidneys and intestines. From the latter a sufficiently large amount is excreted so that if intestinal disturbance is present marked toxic oxidation products are produced and when absorbed these lead to a cumulative effect if the intervals are too short and the function of this organ impaired.

The reaction following the use of salvarsan may be divided into immediate and delayed.

I. Immediate. The commonest symptoms are flushing of the face, cyanosis, a sense of fulness in the head and precordial distress with slight dyspnoea. They usually come on during the administration, may be regarded as anaphylactoid in character, and last but a few minutes. Many patients complain of feeling weak or enervated for the next day or two. More rarely patients are met with in whom vomiting occurs during the administration. In a case under treatment this takes place after 15 or 20 cc. of the solution are introduced. When the attack has passed off the remainder of the dose is taken without trouble. A psychical element is probably present in this case. Occasionally attacks of severe pain in the lumbar region come on during the flow of the drug and necessitate its interruption. After half an hour or so it passes off, the patient experiences no further inconvenience, or he may after an hour or more have a chill with temperature and vomiting. These reactions usually come on after several injections have been given.

II. Delayed. The symptoms appear after 24 hours, 3 days or longer. Those after 24 hours are usually gastro-intestinal, pre-

ceded by a chill or chilly sensation and are characterized by vomiting and diarrhoea with a temperature. In another type there is simply malaise for a few days and then the patients become actively ill with vomiting, fever and a rash or jaundice, the latter the result in all probability of the action of the arsenic on the liver cells. Rarely suppression of the urine is encountered and this may be attributable to the direct action of the drug on the renal vessels.

As the majority of the reactions come on only after several doses have been given, one should be warned by their occurrence and regulate the interval and dosage accordingly. In cases where a dermatitis has been present the drug should not be repeated within six months or a year. I have seen death follow in a patient where the significance of such a rash was disregarded during intensive treatment with neosalvarsan. The injections were continued and a most extensive exfoliative dermatitis developed, ending fatally. In my own experience there have been two deaths which may be said to have been directly attributable to salvarsan. In the first, a man aged 42, the infection was 9 years old. For this he had had treatment at intervals for 6 years. When seen he presented a tubercular ulcerating syphilide of the face, scalp and left arm. He was given mixed treatment under which the eruption disappeared. On December 30th, 1914, he received 0.35 gm. salvarsan, January 11th, 1915, 0.4 gm., January 22d, 0.4 gm. After the last treatment he had a slight reaction and a change was made to neosalvarsan, 0.6 gm., on February 10th, 1915, which was repeated February 20th, 1915. Three days later he developed a temperature of 102 to 104 degrees Fahrenheit and a generalized dermatitis which partially subsided after a week and then recurred with increased intensity. It involved the entire cutaneous surface, the integument became thickened, leathery-like in consistency and pigmented. After a few days abscesses developed in various parts of the skin followed by a recurrence in temperature and rapid heart action. These abscesses were opened and drained but in spite of all the care which could be given the patient death ensued. In this case death could be primarily ascribed to the salvarsan dermatitis and secondarily to the sepsis which followed the cutaneous involvement. The urine showed on March 13th, a marked trace of albumin with a few blood and pus cells and a few epithelial casts. On the 23d only a trace with a few hyalin casts. It should be added that the patient was markedly alcoholic.

In the second case a woman at the City Hospital, treated in 1911 for an early malignant infection, after the second dose developed suppression of the urine, marked reduction of the blood pressure, vomiting and collapse within 24 hours after administration. Autopsy made by Dr. Larkin revealed degenerative changes in the kidney epithelium, in the suprarenal bodies and fatty degeneration of the liver cells.

As mercury has a great affinity for the renal cells the kidney is one of the prime organs to suffer in mercurial intoxication. Hence it is important in the administration of the drug to determine the renal eliminating formation and to examine the urine from time to time. From their studies of the various preparations of mercury Schamberg, Kohlmer and Raiziss concluded that the toxicity of the different salts is proportional to the amount of pure mercury contained. After absorption the drug circulates about as a compound of mercury albuminate and sodium chloride, excretion taking place chiefly in the faeces and only to a small extent in the urine. It is believed that a definite ratio is maintained between the amount excreted by the kidneys and that present in the general circulation and passing through the renal vessels. The rapidity with which it appears in the urine is taken as an indication of the rapidity and intensity of its effects in the body, its elimination corresponding with its cessation of activity. Its excretion continues for months and it may appear again after the urine has become free, from which is deduced that mercury is stored up in the different organs and unless elimination keeps pace with absorption poisoning will result. (Meyer and Gottlieb[7].)

When inunctions are employed mercury appears in the urine from the first day on. Elimination gradually increases to a certain point, then remains for weeks nearly constant and after cessation of treatment falls again gradually[7]. The method is very efficacious but unless in the hands of a professional rubber uncertain. Its disadvantages are constant supervision and filthiness.

When given orally the amount of mercury in the urine shows marked variations from day to day due apparently to varying conditions affecting absorption from the intestine. With suddenly increased absorption there is danger of mercurialism[7].

The results of the treatment of syphilis by intramuscular injections of mercurial salts are more rapid after the use of a soluble than an insoluble preparation. The soluble salt is more rapidly

efficacious because it is possible to more quickly mercurialize the patient owing to the more rapid absorption and less local reaction. Excretion begins at once and if given each day elimination rises gradually and regularly, the amount gradually decreasing when stopped. Unfortunately to be efficient the injections should be given daily in doses of 1/10 to 1/5 of a grain. This of course can be done in hospital wards where patients are under continuous observation but in dispensary practice and private work it is found to be impracticable because of the frequent visits necessitated. For this reason the insoluble salts have come into use. They form a depot of absorption and require to be administered only at weekly intervals. The rate of absorption is of course much slower, the local reaction more intense and the therapeutic effect slower and less reliable. From animal experiments Schamberg, Kohlmer and Raiziss[6] found that at the end of 6 or 7 weeks almost 50% of the mercury of insoluble preparations may be unabsorbed at the site of injection. Cases have been reported where patients weeks or months after treatment suffered from mercurial poisoning when sudden absorption from several foci took place. The elimination curve does not indicate a gradual regular saturation, but maximal elimination occurs on the day of injection and sinks immediately, rising with each new injection. We are now treating all of our cases at the City Hospital with soluble preparations and we find that some of the most refractory rashes like the early follicular syphilide disappear in from two to three weeks even where salvarsan is not given. They are also especially valuable in cerebro-spinal syphilis where a rapid effect is desired.

Conclusions.

The fate of the syphilitic individual depends upon the early diagnosis of his infection and the intensity with which treatment is carried out in the first six months. In the accomplishment of this purpose the modern aids to diagnosis have rendered great service. The dark field illumination furnishes a valuable means of corroboration in all suspicious genital sores and assists in determining the nature of extragenital lesions which may simulate chancre. It should be employed in every case of chancroid to confirm or rule out the possible coincident infection with the treponema pallidum.

The Wassermann test fills a large field of usefulness not only as a diagnostic medium but as a guide to the effect of treatment and

criterion of cure. It is of especial value in all conditions of obscure etiology referable to the cardio-vascular system, cerebro-spinal system or viscera in which syphilis might be a factor, and in cases with an indefinite clinical picture such as neuraesthenia, febrile attacks, rheumatic pains, etc. Its interpretation is of great importance and requires as much training and experience on the part of the practitioner as does the interpretation of the physical signs.

The examination of the spinal fluid enables us to determine the activity of the luetic process in the brain or cord, to distinguish the various pathological types affecting the central nervous system and in many cases to differentiate between these and non-syphilitic affections. Recent investigations have shown that an analysis of the spinal fluid is not complete unless the Lange or colloidal gold test is performed in addition to the Wassermann reaction and a cytological and chemical examination. Its chief usefulness lies in distinguishing true paresis from types of cerebro-spinal syphilis which simulate it and in diagnosing incipient cases before the clinical syndrome is established. This affects chiefly the prognosis as our main hope lies in the early diagnosis and treatment of these cases, for where degenerative stigmata are already present the outlook is not so encouraging, for sooner or later relapses occur.

In primary syphilis where the spirochaetae are demonstrated and the Wassermann reaction is negative it is possible to cure syphilis with salvarsan alone. It cannot be determined how many doses are required and as there may be a dissemination of spirochaetae even in the presence of a negative Wassermann reaction it is better therefore to err on the side of safety and to give at least 8 or 10 doses and follow this with mercury for perhaps six months.

In secondary syphilis where the early rash is present and the Wassermann positive it is better to precede the salvarsan with several injections of a mercurial salt, preferably a soluble one, on account of the economy of time. In this way an effect is produced on the spirochaetae and when salvarsan is given the temperature reaction and an intensification of the rash, that is, a Herxheimer reaction, can be avoided. After the salvarsan is begun the treatment is to be continued in the manner outlined in the body of the article. The dermatologist and syphilologist should keep in mind the possibility of the involvement of the nervous system in secondary syphilis and a complete status should be made when the patient comes under observation so that this record can be compared with

any subsequent developments. In this way we are often enabled to detect the very earliest changes which manifest themselves objectively in the nervous system. The most frequent are irregularity of the pupils, persistent headache, and optic neuritis or auditory disturbance.

In latent syphilis with a positive Wassermann reaction an investigation should be made of the cardio-vascular and of the nervous systems or of previous involvement of any of the viscera, as for instance, syphilitic hepatitis. In cardio-vascular syphilis the prolonged use of mercury in connection with potassium iodide is probably of more value than the haphazard use of occasional doses of salvarsan. In other words, in tertiary syphilis with a persistent positive Wassermann reaction the beneficial effects of potassium iodide cannot be too strongly insisted upon. In bone and periosteal lesions attended by severe pain there is no drug in the pharmacopoeia that produces so rapid an effect in relieving the pain and reducing the neoplasm.

The criteria of cure are a negative Wassermann reaction for at least a year, continuing so after a provocative injection of salvarsan and a normal spinal fluid, with the exceptions which have been noted.

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TABLE I.—RESULTS OF TREATMENT IN CASES OF EARLY INFECTION.

Case.	Duration of infection.	Treatment.							Serological result.	Clinical or serological relapse.	Provocative salvarsan.
		Begun.	Ended.	Amount and kind.							
				Salvarsan injections.	Mercury.			Mixed.			
					Injections.	Rubs.	Oral.				
J. M.	2 months	July 15, 1910	July 25, 1911	1	19	35	3 months	...	June 9, 1911—	None	June 24, 1914—
G. S.	9 weeks	Feb. 2, 1911	Oct. 1, 1913	2	..	60	3½ months	...	Dec. 6, 1911—	"	Dec. 17, 1913—
C. E.	2 months	Feb. 11, 1916	Sept. 15, 1912	2	One	and a half	years	...	April 26, 1911—	"	June 17, 1914—
W. C.	2 months	Nov. 17, 1910	Dec. 22, 1910	3	..	..	..	...	Feb. 4, 1911—	"	Dec. 23, 1914—
H. N.	2 weeks	Nov. 20, 1911	July 9, 1912	4	17	..	..	...	Oct. 6, 1912—	"	Mar. 28, 1914—
B. S.	10 weeks	Nov. 24, 1913	Dec. 19, 1914	17	47	..	..	...	Sept. 14, 1914—	"	Dec. 6, 1915—
A. N.	7 months	Sept. 27, 1913	Sept. 9, 1914	17	41	..	..	...	Oct. 9, 1914—	"	Dec. 28, 1915—
J. G.	6 weeks	Feb. 19, 1908	Oct. 21, 1910	..	31	..	1 year	1 month	Jan. 25, 1911—	"	Feb. 26, 1915—
S. W.	6 weeks	Dec. 30, 1910	July 27, 1911	2	13	10	..	...	June 11, 1913—	"	
R. Y.	3½ months	Jan. 14, 1911	July 9, 1912	7	..	..	..	...	Mar. 11, 1911—	"	
G. B.	5 weeks	April 10, 1911	Jan. 15, 1912	3	..	9 weeks	2 months	...	May 4, 1912—	"	
T. C.	1 month	Oct. 21, 1912	Nov. 9, 1912	4	..	..	..	...	Always—	"	
H. C.	4 weeks	Jan. 23, 1914	Oct. 30, 1914	10	21	..	..	...	April 18, 1914—	"	
G. C.	5 weeks	July 31, 1914	April 14, 1915	10	24	..	..	...	Nov. 18, 1914—	"	
C. A.	6 weeks	Dec. 15, 1913	Oct. 17, 1914	6	25	..	..	...	Always—	"	
J. C.	2 months	June 13, 1914	Mar. 2, 1915	9	25	..	..	...	Sept. 17, 1914—	"	
H. N.	4 months	Nov. 16, 1913	May 29, 1914	13	13	..	..	...	May 27, 1914—	"	
R. G.	8 weeks	Aug. 16, 1913	June 2, 1914	12	19	..	..	...	June 13, 1914—	"	
W. C.	6 weeks	Aug. 15, 1905	Oct. 6, 1909	..	50	..	7 months	6 months	Oct. 24, 1913—	"	

TABLE II.—RESULTS FOLLOWING PROVOCATIVE INJECTION.

Case.	Date of infection.	Wassermann before treatment.	Treatment.						Wassermann.	Clinical or serological relapse.	Provocative salvarsan.
			Begun.	Ended.	Amount and kind.						
					Salvarsan injection.	Mercury.					
						Injection.	Rubs.	Oral.			
P. A.	1886	4+	Dec. 2, 1909	June 18, 1912	1	61	...	...	Dec. 6, 1913—	None	Jan. 14, 1914++++
J. B.	1897	(?)	1897	1900	..	...	...	2½ years	Oct. 30, 1912—	"	Nov. 12, 1912++++
C. M.	1910	(?)	Oct. 19, 1914	Feb. 1, 1915	..	50	...	...	April 3, 1915—	Has tabes	April 14, 1915++++
J. A.	1901	(?)	1901	1905	..	1½ years	3 years	...	Mar. 15, 1916±	Gummata	Mar. 23, 1916++++
E. K.	Hereditary, 7 years old	±	No treatment Parents syphilitic	No symptoms	..	...	...	...	.....	....	Provoc. KI Oct. 7, 1915 Wassermann Mar. 1, 1916++++
J. C.	1890	(?)	1890	1899	..	...	8 years	6 months	1909—	None	Jan. 23, 1912—
W. H. S.	June, 1913	4+	Dec. 2, 1913	Oct. 1, 1914	16	44	...	...	Nov. 24, 1914—	"	Sept. 12, 1915—
T. P.	(?) third stage	4+	Sept. 29, 1913	April 11, 1914	16	42	...	...	May 11, 1914—	"	Oct. 20, 1915—
J. E. H.	Feb. 2, 1914	4+	April 14, 1914	Dec. 1, 1914	16	38	...	...	Jan. 25, 1915—	"	Nov. 27, 1915—
S. D.	(?) third stage	4+	Sept. 24, 1913	Sept. 15, 1914	17	49	...	...	Oct. 16, 1914—	"	Feb. 9, 1916—
G. E. G.	(?) third stage	4+	May 19, 1914	July 9, 1915	13	56	...	...	July 9, 1915—	"	Dec. 20, 1915—
M. R.	May, 1914	4+	July 8, 1914	June 15, 1915	15	46	...	...	Feb. 3, 1915—	"	Dec. 19, 1915—
B. S.	Miscarriages	4+	Dec. 26, 1913	Feb. 30, 1915	19	47	...	...	Mar. 2, 1915—	"	Feb. 7, 1916—
B. S.	Sept., 1913	4+	Nov. 24, 1913	Dec. 1, 1914	17	47	...	...	Sept. 14, 1914—	"	Dec. 6, 1915—
C. B.	April, 1914	4+	Dec. 29, 1914	Dec. 15, 1915	15	45	...	...	July 22, 1915—	"	Feb. 8, 1916—
A. N.	Jan., 1913	4+	Sept. 27, 1913	Sept. 9, 1914	17	51	...	...	Oct. 9, 1914—	"	Jan. 24, 1916—
A. Mc.	May, 1914	4+	July 12, 1914	July 15, 1915	17	42	...	...	Feb. 15, 1915—	"	Jan. 3, 1916—
T. M.	1908	4+	Oct. 21, 1912	July 7, 1913	9	22	...	...	Sept. 11, 1913—	"	Dec. 27, 1915—

TABLE III.—INTRACTABLE REACTIONS AFTER PERSISTENT TREATMENT.

Case.	Date of infection.	Wassermann before treatment.	Treatment.					Wassermann after treatment.	Clinical relapses during treatment.	Remarks.
			Amount and kind.				Duration.			
			Salvarsan injections.	Mercury.		Mixed.				
				Injections.	Rubs.					
W. Z.	Nov., 1911	++++	14	45	...	....	1½ years	++	None	Clinically negative.
B. H.	April 26, 1913	++++	16	36	...	....	1 year	+	"	Clinically negative.
F. G.	April, 1912	++++	20	26	...	....	1½ years	±	"	Clinically negative.
A. R.	1909	++++	22	36	4 months	4 months	2 years	++++	"	Clinically negative; spinal fluid negative.
W. W.	1899	++++	16	31	...	8 months	2½ years	++++	"	Has remains of hepatitis.
L. H.	Dec., 1912	++++	15	101	4 months	18 weeks	2¾ years	++	"	Has aortitis.
I. D.	Mar., 1913	++++	12	72	...	6 months	2½ years	+	"	Has aortitis.
J. B.	Denied	++++	17	10	...	6 months	1½ years	++++	"	Large aneurysm present.
R. H.	1907	++++	23	30	88	16 weeks	2 years	++++	"	Optic atrophy; spinal fluid positive.
F. M.	1903	++++	9	32	...	....	7 months	++++	"	Tabes; spinal fluid positive.
G. M.	1902	++++	20	60	6 months	1 year	2½ years	++++	"	Spinal fluid positive; cerebro-spinal syphilis.
								++++		
E. R.	1904	++++	31	40	...	....	1½ years	++++	"	Has paresis; spinal fluid positive.
M. D.	Congenital 29 years ago	++++	18	36	...	2 years	3 years	++++	"	Remains of keratitis; deafness; spinal fluid negative.

THE TREATMENT OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM.

HOMER F. SWIFT, M.D.,
New York City.

In order to discuss treatment of syphilis of the central nervous system it is essential to orient ourselves in the various problems which this disease presents.

It is now well established that spirochetes circulate in the blood of practically all patients in the late primary and early secondary stages, and during this period the central nervous system is frequently involved. In fact, with the early and almost universal dissemination of the infectious agent it is difficult to conceive how any organ escapes infection. It is not alone the presence of the spirochetes, but the reaction of the tissues towards them which determines the type of lesion.

It is now recognized that spirochete can lie dormant in the tissues, in latent cases, with practically no cellular reaction about them. Different observers report wide variation in the relative frequency with which the cerebrospinal fluid shows evidence of alteration in the secondary period. Ravaut[1] found abnormalities, with pleocytosis or globulin excess or both, in 67% of cases, Altman and Dreyfus[2] in 66%. Gennerich[3] states that at some time, either before or during intensive salvarsan treatment, 90% of his cases in the secondary period showed some abnormality of the cerebrospinal fluid. Ellis and I found only 33% of abnormal fluids in untreated patients in the secondary period, but had the fluids in all patients in the secondary period been included in our statistics the percentage would be somewhat higher.

From the above observations, it is evident that infection of the central nervous system occurs in a large proportion of cases of secondary syphilis. Since we know that only a small proportion of syphilitic patients show nervous involvement in later years, it is evident that in many cases this infection must undergo spontaneous resolution. This phenomenon corresponds with the course of syphilis elsewhere in the body and is probably due in part to a tissue immunity which develops as a result of prolonged contact

between parasite and host. As a result of this tissue immunity the secondary eruption disappears, and cutaneous relapses may never recur even in untreated patients. If, however, cutaneous manifestations do recur they become more and more localized, tend to group and to involve deeper structures with final gummatous changes.

A similar process appears to occur in the central nervous system. Following the initial inflammation, the organisms deposited in the meninges during the period of spirochetemia are usually destroyed, but in some cases they remain latent only to become active after a period of months or years. This is the usual course of syphilitic infection in untreated or poorly treated cases. The character of the picture may, however, be altered by the institution of intensive treatment. It has long been observed that cases of primary syphilis, relapsing after unsuccessful attempts at abortive treatment with mercury, are liable to show severe skin lesions. Similar deep nodular or ulcerative lesions are frequently seen in the relapses following inadequate treatment. This phenomenon of increased severity noted in relapsing lesions of the skin occurs also in the central nervous system, and explains the occurrence of meningitis with cranial nerve paralysis in many of the inadequately treated cases of secondary syphilis. In these patients the greater part of the infecting organism has been destroyed by the remarkable spirocheticidal action of salvarsan. This has, moreover, been accomplished so rapidly that the usual tissue immunity which develops as a result of prolonged contact between parasite and host is lacking. As a result a small focus of spirochetes, tucked away safely in the tissues of the central nervous system, thus escaping the spirocheticidal action of the salvarsan, can develop in the susceptible host with great rapidity and severity. The severity of the meningitis is evidenced by the cerebrospinal fluid, which shows a marked pleocytosis, considerable globulin excess, and usually a strongly positive Wassermann reaction. The Wassermann reaction in the blood is frequently negative, showing how well the active syphilis is limited to the central nervous system. The failure to recognize this possibility of active meningitis in the early stages of syphilis with a negative Wassermann reaction in the blood, may result in the failure to resume treatment at a most critical period. It should be emphasized that the development of this condition is due to inadequate intensive treatment and that a few doses of salvarsan, without con-

tinued treatment, may result in more severe nervous manifestations than if milder therapy had been applied.

The recognition of the early involvement of the central nervous system is important not only because of the possibility of the development of an early meningitis but also from the standpoint of prophylaxis of the later and more destructive conditions. The best treatment of brain gummata, tabes and paresis will always be their prevention.

Before starting treatment in any case it is well to try to recognize the character of the involvement, for the subsequent therapy is to a certain extent determined by the type of manifestation. These manifestations depend upon the tissues involved, and upon the reaction of those tissues to the irritative effect of the spirochetes. The disease may implicate the meninges, blood vessels or parenchyma. While it is conceivable that any one of these structures may be affected alone, still the intimate relation of one structure to the other makes it almost impossible for one to be diseased without the others sharing to a certain extent in the pathological process. There is, however, a type of nervous disease due to syphilis in which the infection seems to involve the vessels in the form of an endarteritis. In this instance the cerebrospinal fluid shows little if any abnormality, and the symptoms are referable to the arterial sclerosis of the cerebral vessels rather than to actual interstitial or parenchymatous disease. The response of this type of case to treatment depends upon the extent to which the endarteritis can be favorably affected, and not upon the resolution of a syphilitic exudate in the meninges.

Following the demonstration of the treponema pallidum in paretic brains a new classification of lues of the brain and cord has arisen. This comprises (1) interstitial types, which include the lesions previously classified under cerebrospinal syphilis; and (2) parenchymatous types, which include paresis and tabes dorsalis.

In both the interstitial and parenchymatous forms, the one common lesion is the perivascularitis which may vary to a wide degree, from a simple mantling of the vessel, to a collection of cells in the form of miliary gumma, and when combined with a similar process in the meninges may result in large gumma formation. In the interstitial forms which include meningitis, meningo-arteritis and gumma, the disturbance in function is due either to an actual destruction of the nervous element or to a cutting off of nutrition to

the nerve tracts and centers. This latter condition may be brought about by the narrowing of vessels and compromising of the lymphatic spaces, to the edema surrounding active inflammation, and to pressure from the tumors. In fact the remarkable improvement of many of these cases under treatment can be explained only on the basis that the pathological process has been largely limited to the vessels and meninges. In the parenchymatous forms the outstanding picture is degeneration of nervous elements, combined with symptoms of irritation of these structures. Unfortunately it is impossible to examine microscopically the tissues in these parenchymatous forms until late in the disease when the degeneration is far advanced. But even at this time perivascularitis and focal meningitis are usually seen, and it does not seem unreasonable to consider that much of the degeneration is secondary to a disturbance of the nutrition of the cell or axis cylinder, which has resulted from a blocking of the perivascular, perineural or perineuronal lymph spaces by the cellular exudate.

In paresis the presence of the spirochete in the brain substance may by the liberation of toxins result directly in the death of the cell. In tabes dorsalis, however, the active inflammatory process is not usually found in the most obviously degenerated areas, viz., the columns of Goll and Burdach, but rather in the dorsal roots and in the meninges surrounding them. An example of the earliest stages of tabes is the interesting case of Larkin[5] in a patient with "sciatica," girdle pains, pleocytosis and positive Wassermann reaction in the cerebrospinal fluid, who died from a ruptured aortic aneurism and whose post mortem showed insular sclerosis of the posterior nerve root, with accompanying syphilitic meningitis, but no column degeneration.

From the examination of the retina and optic nerves of many cases of optic atrophy in tabetics and paretics, Stargardt[6] concluded that the atrophy is secondary to a round cell infiltration of the intracranial portion of the optic nerve and the chiasm. In those cases with a segmental optic atrophy there was only a partial infiltration of the optic nerve. He argues against the view that tabetic optic atrophy is a system disease due to a toxin, but believes rather that it is an example of the reaction of the nervous tissue to the spirochete, for in several of his cases the auditory and olfactory nerves were similarly infiltrated. Spiller[7] showed that the essential lesion in tabetic oculo-motor paralysis is due to a round

cell infiltration in the oculo-motor nerves at their point of emergence from the medulla, which he thinks is probably secondary to the pial infiltration in this region. He considers that the nuclear degeneration is usually secondary to the inflammation of the nerve stem. Thus it appears that the classification of the various tabetic atrophies as primary is only an attempt to explain them in terms of the older opinion that these diseases were parasyphilitic in nature. As a matter of fact they all appear to be secondary to a chronic syphilic meningitis.

Chronicity is probably an important element in the development of parenchymatous syphilis. The outstanding symptoms of most cases of tabes or paresis develop from the tenth or twelfth year after the primary infection. Upon careful questioning of many of these patients, it will be found that some single symptom, such as pain or isolated nerve paralysis, often transitory in character, has occurred years previously, and their nature is often recognized only when the disease is well developed. These facts point to the probability that a low grade inflammation with subsequent atrophy has been going on for years and only after a sufficient number of tracts or centers are involved to interfere with the patient's usual activities does he seek the aid of the physician. On the other hand, the majority of cases of the interstitial type develop in the first three years after infection. The course is more rapid and the symptoms appear with greater violence, no doubt due to the fact that there is a more extensive and rapid development of the meningeal and perivascular exudate.

In both tabes and cerebrospinal syphilis, then, we are dealing with diseases of a similar nature. The variation in the manifestations seems to depend upon the difference in the rapidity and degree of development as well as upon the localization of the inflammatory process. In tabes the infiltration being less intensive and slower, the picture of degeneration is brought more vividly into the foreground. The spinal fluid in the two diseases is practically the same, even to the type of curve in the gold reaction. Both also respond to specific treatment in much the same manner, although at a different rate, and while the symptoms due to irritation are improved, those due to degeneration are little if any affected.

In paresis, on the other hand, we appear to be dealing with a disease which is not strictly comparable with the two just discussed. There are certain points of similarity, viz., in the men-

ingitis and perivascularitis. The direct action of large masses of spirochete in the substance of the cerebral cortex may possibly result directly in the destruction of cortical cells and fibres. The peculiar type of curve in the gold reaction, however, points to some essential difference between this disease and tabes. The difference in response to treatment is also most striking. While most cases of tabes will show the favorable influence of treatment both in the spinal fluid and in marked and persistent clinical improvement, the response of most paretics to a similar, or more intensive treatment, is much less noticeable, and the ultimate results are usually discouraging. Whether this difference in response is due to difference in accessibility of the active lesion, or to the fact that in paresis the disease attacks portions of the central nervous system, which are more essential to the orderly carrying on of vital functions, are questions which are as yet unanswered.

It goes without saying that the best preventive of syphilis of the central nervous system is the prophylaxis of syphilis, but this problem is far from solved. Next in importance is the proper treatment of syphilis in the early stages. It should be emphasized at this point that no case should be released from treatment until the cerebrospinal fluid has been shown to be normal, in so far as pleocytosis and Wassermann reaction are concerned. Whether a slight excess of globulin is an indication for continuation of treatment, if all other abnormal elements are absent, is still an open question. In a number of patients with meningitis in the secondary period, whom we have followed for several years, the globulin is still in excess, although all other evidence of the disease has been absent for three or more years.

Even with the present diagnostic methods and several effective therapeutic agents, it is safe to say that a fair proportion of patients with syphilis are poorly treated and probably a majority of them are released without lumbar punctures. The failure of many patients to be followed until cured is due to several causes. First, the patients fail to realize the importance of proper treatment in the prophylaxis of later disease and discontinue their treatment of themselves. Second, there is still a surprising lack of facilities in dispensaries for the proper treatment of syphilis. Third, many physicians fail to realize the long systematic course that is required to eradicate the disease completely. Fourth, there are many cases of innocent syphilis and syphilis with slight, if any early mani-

festations which go untreated and later develop serious nervous lesions. (Table I.)

TABLE I.

Mattausehek and Pilcz — Total cases 4134

Developed paralytica dementia	198 = 4.8 per cent.
" tabes dorsalis	113 = 2.7 "
" cerebrospinal lues	132 = 3 2 "
Total	443 = 10.5 "

Effect of Treatment.

	None.	1 course.	Repeated energetio
Number of cases	100	134	924
Developed G. P.	25 = 25 per cent.	31 = 23.1 per cent.	30 = 3.2 per cent.
" tabes	11 = 11 "	16 = 11.9 "	25 = 2.7 "
" cerebrospinal lues	3 = 3 "	21 = 15.6 "	71 = 7.6 "

	Poorly treated 1880–84.	Better treated 1895–99.
Number of cases	617	1139
Developed G. P.	60 = 9.7 per cent.	37 = 3.2 per cent.
" tabes	22 = 3.5 "	16 = 1.4 "
" cerebrospinal lues	15 = 2.4 "	28 = 2.4 "

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While the incidence of cerebrospinal involvement in syphilis varies in different races and in the different sexes, the experiences of Mattauschek and Pilcz[8] is representative. These authors followed 4134 cases of syphilis in officers in the Austro-Hungarian army who were infected between 1880 and 1900. These cases were followed until 1912. The results of these investigations are shown in Table I. A striking feature of the table is the difference in the per cent of cases that developed tabes and paresis who were untreated or poorly treated compared with those who had been energetically treated. Practically a quarter of the poorly treated cases developed paresis contrasted with a little over 3% of those who were well treated. Similarly from 11 to 12% of the poorly treated ones developed tabes, while only a fifth of this proportion of well-treated patients developed this disease. A single course of treatment seemed to increase the liability to the cerebrospinal form of lues. This observation is of added interest in view of our present knowledge of the results of insufficient salvarsan treatment on the development of cerebrospinal syphilis already discussed in an early part of this paper. A similar parallelism between early efficient treatment and diminished incidence of tabes and paresis is seen in the last part of the table. In the period between 1880 and 1884, the treatment was relatively insufficient, while in the period between 1895 and 1899 there was an improve-

ment in the general treatment of the disease with a corresponding decrease in the incidence of parasyphilis. It is striking that the incidence of cerebrospinal syphilis in the two groups is the same.

If the difference between poor application of mercury and fairly efficient application is so marked, it is reasonable to expect that under the modern intensive treatment with both mercury and salvarsan the incidence of parasyphilis should be even more markedly reduced. From a simple, economic point of view the State should provide for the proper treatment of early syphilis, for upon the State eventually falls the cost of caring for the paretic and, to a less extent, for the tabetic.

From the standpoint of prophylaxis of tabes or paresis it is also important to realize that they frequently develop slowly and that signs or symptoms are often present for years before the disease is fully manifest. Lately more attention has been directed to the monosymptomatic form of syphilis of the central nervous system. Some authors claim that these forms are more frequent to-day than formerly and that tabes is assuming a milder character; but it is more probable their detection is due to refinement in diagnosis. While fairly numerous cases are reported in which the monosymptomatic forms remained free from further symptoms for many years in spite of lack of treatment, it is wiser to regard all such cases as being early forms of late serious disease. Years ago Erb called attention to the importance of ophthalmoplegia interna as a forerunner of tabes or paresis and he has followed several cases from the appearance of a simple eye lesion to the fatal ending in paresis. Many patients with tabes give a history of a transitory squint which was present years before any other symptom. Often the condition has improved after the administration of a small amount of iodides or mercury and the patient has been allowed to escape from further observation. Auditory nerve lesions are also described early in tabes as well as in cerebrospinal syphilis. These patients usually consult the otologist. It is important for the specialist to realize that these isolated nerve lesions are a part of the general disease, syphilis of the central nervous system, and that they are usually manifestations of a basilar meningitis. Surgeons also see early manifestations in abdominal disturbances. Nuzum[9] recently reported that among a thousand cases of tabes admitted to Cook County Hospital, eighty-seven had previously undergone laparotomy because of the mistaken diagnosis of their abdominal pain. It is important to remember that gastric crises, either mild or severe,

may be present as the first manifestation of tabes for years before full development of the disease. Other single symptoms which are often present for a longer or shorter period are bladder disturbances, lightning pains in the leg and "rheumatism." The general practitioner or the specialist should recognize the nature of these symptoms and place the patient under proper treatment, for it cannot be emphasized too strongly that prevention of degeneration is worth vastly more than the treatment of symptoms once they have fully developed.

The examination of the blood and cerebrospinal fluid is of the greatest help in clearing up the diagnosis in doubtful cases, and to a certain extent in determining the type of syphilitic involvement of the central nervous system. While these examinations are of great value, they do not replace but only complement a careful clinical examination. I cannot do better than quote Miller[10]: "The value and interpretation of any laboratory method should always be based upon the most careful clinical study of the cases in which it is applied," and also "Any normal reaction in the cerebrospinal fluid may be present or absent in any luetic involvement of the brain or spinal cord." There are certain combinations of reactions which occur with sufficient frequency in certain conditions to render such findings highly significant. An increase in globulin is found in most cases of any type; it is most marked in paresis, but may be equally intense in secondary meningitis. Pleocytosis is usually the most intense in meningitis in the secondary stage, but counts above 100 are not infrequent in later cerebrospinal syphilis, tabes and paresis. The type of curve given by the Lange gold reaction in cerebrospinal lues and tabes is of confirmatory value, but its great field of usefulness seems to be in differentiating paralytica dementia from these two conditions. The fact that the fluid from a patient with a clinical diagnosis of tabes, or cerebrospinal syphilis, gives a paretic curve does not militate against the reaction, for it is well known that between 10 and 15% of tabetics develop paresis and at times it is impossible to differentiate between cerebral syphilis and paresis. If future observations confirm what now seems probable, viz., that a paretic curve obtained with the spinal fluid of patients clinically not paretic points to a possible development of this disease, it will be of importance in prognosis and of value in determining why symptoms of mental disorder appear in spite of vigorous and prolonged treatment.

At this point, it is well to emphasize the value of constant methods in making the various tests on the cerebrospinal fluids. Dilutions for cell counts should be made immediately. The necessity of proper solutions for the gold test have been pointed out by Miller[11] and his co-workers. Of no less importance is the titration of the strength of the Wassermann reaction in the spinal fluid. The designation of four plus, or negative Wassermann reaction, in the fluid means but little unless we know the amount of fluid that was used in obtaining these readings. This is especially true when the effect of treatment is being estimated. For example, if 0.2 cc. or 0.4 cc. has been the only amount used to test the fluid, a relatively mild treatment may change the reaction to negative. On the other hand, if only 1 cc. has been used, a more intensive treatment may not affect the reading although, as a matter of fact, the reaction may be much weaker. The only way to judge accurately of the effect of treatment on the reaction is to test the fluid with diminishing amounts corresponding to values between 2 cc. and 0.2 cc. in the original Wassermann test (smaller amounts if necessary) and determine the point at which the reaction is completely positive. If then with a given amount of treatment, the positive point has moved from 0.2 cc. to 0.6 cc., or higher, we know that the treatment is having some effect. This, of course, presupposes that constant methods are used at different times, for if a very sensitive method is used at one time and a comparatively unsensitive one at another, the relative value of the two tests is lost.

The problem of treatment of syphilis of the central nervous system is complicated by the peculiarities of the subarachnoid space which, in addition to the larger spaces and cisterna, is directly continuous with the perivascular, perineural and perineuronal lymph spaces. It does not seem unreasonable to suppose that the infection is carried by the cerebrospinal fluid along these channels, and the various meningeal and perivascular lesions can be most easily explained in this way. Frühwald[12] and Zaloziecki, in a review of their own cases and of the literature, have shown that the fluid is occasionally infectious in all stages, from the secondary period to tabes and paresis.

The reaction to the spirochete is meningitis and perivascularitis. It is probable that the nerve cell and fibres obtain their nutrition to a considerable degree through these spaces, hence plugging of them with exudate not only compromises the nutrition of these structures, but also probably increases the difficulties with which therapeutic

agents are brought into contact with the exudate. At present it seems almost superfluous to recite the numerous experiments which prove the separateness of the subarachnoid space from the general lymphatic and blood vascular systems. Anti-bacterial immune bodies, vital stains and most drugs, when administered by mouth or parenterally, do not reach the subarachnoid space in demonstrable quantities. It is true, however, that many drugs, given either by mouth or subcutaneously, do act on the central nervous system, but these drugs administered subdurally act in much smaller quantities. Many years ago, Lewandowsky[13] showed that strychnine when injected intraspinally was ten times as effective as when injected intravenously. Similarly sodium ferrocyanide subdurally was potent in one-hundredth the intravenous dose. The action of both drugs was at first local and then general, showing that they were rapidly diffused through the cerebrospinal fluid.

In many cases, the general administration of mercury, iodides and salvarsan affects favorably the course of syphilis in the cerebrospinal axis. This favorable influence is especially marked in the early forms of the disease. The tendency, however, of cerebrospinal syphilis to relapse in spite of energetic mercurial and iodide treatment has long been noted by syphilographers and neurologists, and the failure of most cases of tabes to respond to the antiluetic treatment of the presalvarsan era made therapeutic nihilists of most neurologists. Even the brilliant clinical improvement of most cases of cerebrospinal syphilis and tabes after salvarsan intravenously, has not been followed by a parallel improvement in the cerebrospinal fluid. Dreyfus,[14] who gives courses of salvarsan of 4-6 gms. combined with 10 to 12 injections of calomel or gray oil, notes that many such courses are necessary to eliminate all signs of the disease. In only three out of one hundred and twenty-five cases of cerebrospinal syphilis did the fluid become normal after one or two courses. Gennerich,[15] who is famous for the intensity of his antisyphilitic treatment, says that he feels that all cases with meningeal involvement in any stage should have intraspinal treatment. Many observers report cases of cerebrospinal syphilis of tabes which, having come to a standstill both clinically and pathologically under general treatment, have shown renewed improvement under intraspinal therapy.

The desirability of subarachnoid therapy has been well established. The problem was to find some beneficial therapeutic sub-

stance which could be repeatedly introduced without injury to the delicate nervous tissue, for only by repeated and prolonged treatment can we hope to arrest any form of cerebrospinal lues permanently. Last year,[16] the writer reviewed the use of these various agents and the methods of their administration. Suffice it to say that the preparations which have stood the test of time are (1) the serum obtained from patients shortly after intravenous injections of salvarsan, (2) serum to which small quantities of salvarsan have been added, (3) neosalvarsan in small quantities and weak concentration and (4) mercurialized serum.

The direct application of mercury in the form of albuminate as devised by Byrnes[17] should theoretically be of value, and the reports seem to indicate that if the amount of mercury is kept under the irritating dose beneficial results may be expected from its injection. It is well to call attention to the danger of repeated injections of mercurialized horse serum, which may lead not only to a general anaphylactic state to horse serum, but may cause the meninges to become hypersensitive to the foreign protein, and repeated injections over a number of months may lead to a chronic meningitis similar to the condition we are trying to combat.

The injection of neosalvarsan in concentrated solutions as recommended by Ravaut[18] or even in one pro mille solutions has been proven by numerous observers to be a dangerous procedure since it is apt to be followed by various degrees of urinary retention and incontinence, rectal paralysis, paresthesia of the legs, ataxia and girdle sensations and, in severe cases, by paralysis of the lower extremities and death. A given dose may be well tolerated several times, but later be followed by severe symptoms. Because of the uncertainty of unfavorable sequelae, intraspinal injections of neosalvarsan should be given with extreme caution. Gennerich[15] lately reported that by using very dilute solutions he has been able to avoid these unpleasant symptoms. He, however, warns against the use of more than 0.5 mg. in spinal cord cases, and not over 1 or 2 mg. in patients with paresis or syphilitic meningitis. Personally, I feel that repeated doses of this size are dangerous.

The addition of small quantities of salvarsan to serum as recommended by Ogilvie[19] was devised to give a known amount of salvarsan instead of the uncertain dosage in the serum salvarsanized *in vivo*. Marinesco and Minea[20] have noted that neosalvarsan is less irritating when diluted with serum than when dissolved in water or

saline. Both Ogilvie and Fordyce,[21] however, have noted bladder disturbance and paraesthesia in the legs when more than 1 mg. of salvarsan was added to the serum and now I recommend that the dose should never be over 0.5 mg., usually less. With these quantities intraspinal treatment has been followed by distinctly beneficial results.

The use of the serum of patients withdrawn after intravenous salvarsan injections has been criticized chiefly because of the small amount of salvarsan it contained. We have found that the majority of the sera one hour after an intravenous injection contained 0.01 mg. or more per cc. When 12 to 20 cc. of serum are used each treatment represents the injection of from 0.12 to 0.2 mgs. of salvarsan. As above noted, it is unsafe to inject intraspinally more than a fraction of a milligram of either salvarsan or neosalvarsan. The uncertainty of the dosage is an objection which cannot be overcome unless definite quantities of salvarsan are added.

The "auto-salvarsanized serum" is, however, definitely spirocheticidal and the salvarsan is present in a colloidal combination with the serum which cannot be dialyzed through a celloidin membrane, as can salvarsan alone (Young[22]). Salvarsan in this colloidal state is probably more slowly diffused out of the cerebrospinal fluid, hence is longer in contact with the syphilitic exudates. Moreover, it seems to us that some of the beneficial effect from serum injection may be due to the introduction of the serum per se, for* we have obtained very interesting results from the intraspinal injection of non-salvarsanized both in diminishing pleocytosis and strength of the Wassermann reaction. The amount of the diminution in the Wassermann reaction is shown graphically in Table II. By reading from above downward the initial strength of the Wassermann reaction is indicated, while the reading from left to right gives the strength after treatment. The original strength of the reaction is indicated by the heavy blocks. The number of treatments is indicated in parenthesis. It will be seen that seven out of the eight cases showed a diminution in the strength of the reaction, and in three of them it became negative with 1 cc. fluid. During the period of observation, none of the patients received

* The cases reported in this and subsequent tables were treated at the Rockefeller Hospital in collaboration with Drs. Ellis, Chesney and Stillman. A number of them have been followed at the Presbyterian Hospital.

TABLE II.—EFFECT OF INTRASPINAL INJECTIONS ON WASSERMANN REACTION IN CEREBROSPINAL FLUID.

Non-salvarsanized Serum.

W. R. before treatment.	W. R. after treatment.								No. of injections.
	++++					--	++++	--	
	0.2 c.c.	0.4	0.6	0.8	0.1	0.1	2.0	2.0	
0.2 c.c.	[ ]	1 A	....	....	....	....	....	....	8
0.4 c.c.	....	1 B	....	....	....	....	....	....	7
0.4 c.c.	....	[ ]	1	....	....	....	....	....	13
0.4 c.c.	....	....	....	....	1	....	....	....	12
0.6 c.c.	....	....	[ ]	1	....	....	....	....	4
0.6 c.c.	....	....		....	....	1	1	....	17
0.6 c.c.	....	....		....	....	1	....	1	6
1.0 c.c.	....	....	....	....	[ ]	1	....	....	6
Total 8	....	2	1	1	1	3			

Salvarsanized Serum.

W. R. before treatment.	W. R. after treatment.								No. of injections.
	++++					--	++++	--	
	0.2 c.c.	0.4	0.6	0.8	1.0	1.0	2.0	2.0	
0.2 c.c.	[ ]	....	1	....	....	....	....	....	12
0.2 c.c.		....	....	....	....	1	....	....	11
0.2 c.c.		....	....	....	....	1	....	....	4
0.4 c.c.	....	[ ]	1 A	....	....	....	....	....	4
0.4 c.c.	....		....	1 B	....	....	....	....	8
0.6 c.c.	....	....	[ ]	....	....	1	....	....	8
Total 6	....	....	2	1	....	3			

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any other treatment. In two of the cases, A and B, in which there was little or no effect, the treatment was continued with "auto-salvarsanized serum," from other patients, with more marked diminution in the strength of the reaction, as is shown in part two of the table. The severity of the infection in one of these cases is indicated by the fact that ten months' intravenous and intraspinal treatment was required before the reaction became completely negative. Four other patients were treated with intraspinal injections of salvarsanized serum, and in three of these the reaction became negative with 1 cc. fluid. A resumé of the results in these twelve cases, treated only intraspinally with either normal or salvarsanized serum shows that in half of them the reaction became negative with 1 cc. of fluid, and in the others there was distinct diminution in the strength of the reaction. Two of these patients with gastric crises, Argyl-Robertson pupils, loss of tendon reflexes, bands of cutaneous

anaesthesia, and loss of deep pain sensation have been observed for over three years without any return of their trouble, and the fluids have remained normal. The results in these cases seem to prove that benefit is derived from intraspinal injections of serum. The explanation of these effects may be and probably is theoretical, but so are the objections to the treatment. The experimental facts stand, and the injection of auto-salvarsanized serum is followed by fewer permanent unpleasant effects than result from the intraspinal injection of any other antisyphilitic remedy.

In some patients the pain which follows the injection is so severe that the treatments must be discontinued, but such instances are the exception. The willingness of most patients to return for treatments over long periods is sufficient proof that the method is not too unpleasant for practical application.

A word as to technique. In most of our work at the Rockefeller Hospital, the blood was withdrawn one hour after intravenous treatment, and the serum diluted to 40 or 50% with normal saline, and injected in quantities of 30 to 40 cc. of this dilution. It was thought that the dilute serum was less irritating, but for the past two years at the Presbyterian Hospital, we have bled the patient one half hour after intravenous treatment and injected 15 cc. of whole heated serum without any more reaction than with the older method. Most of the patients now receive both the intravenous and intraspinal injections on the same day, and return to their usual occupations the following day. In this way a minimum of time is required. It is necessary to keep some patients in bed for longer periods. In such instances we try to give the treatments on Saturdays so that the patients may be in condition to work by Monday morning.

It has seemed to us that the treatments are better borne if not repeated oftener than once in two weeks. This is especially true in tabetics or patients with spinal syphilis. In paretics or patients with cerebral syphilis the intervals may be shorter. At times it seems wiser to lengthen the intervals. It is well to bear in mind that a certain amount of irritation always follows the introduction of any foreign substance into the subarachnoid space, and the effect of this should be allowed to disappear before the treatment is repeated. A good rule to follow in any form of treatment of cerebrospinal syphilis is not to push the treatment so hard that the patient's general health is depressed. With each treatment there

should be some improvement in the general condition, at least there should be no regression, for if a depressing treatment is repeatedly added to a more and more depressed condition, the ultimate effect will be injurious rather than beneficial.

The treatment of the several forms of syphilis of the central nervous system presents different problems according to the stage of the disease and the individual patient. One general principle which should always be considered is that in any patient who shows evidence of involvement of the cerebral meninges or brain, salvarsan treatment should be preceded by a short course of mercury to prevent the possible occurrence of a Herxheimer reaction in the region of vital nervous centers. Fortunately such distressing reactions are rare, and can be obviated by proper preliminary treatment. If the presence of gummata is suspected a vigorous course of potassium iodide is often followed by marked improvement. It has seemed to us that the response of cases in the tertiary stage to salvarsan has been more marked and lasting, if the courses of salvarsan have followed treatment with mercury and iodides. Gummatous exudates resolve under this preliminary treatment and the spirocheticidal effect of the salvarsan is more readily brought into play.

In the meningitis of the secondary period the response to alternate courses of salvarsan and mercury has been prompt and permanent in all of our cases. Gennerich[15] is of the opinion that all these cases respond more rapidly to combined intravenous and intraspinal therapy and advises giving two intraspinal treatments after the cerebrospinal fluid has become normal. Following any form of treatment in this condition the cerebrospinal fluid should be examined in two or three months after treatment has been stopped, and every six months for two or more years thereafter to forestall relapses.

In the tertiary forms of the disease, the so-called interstitial forms, alternate courses of mercury and iodides, and of salvarsan are usually followed by decided improvement, both clinical and in the condition of the cerebrospinal fluid. If possible the fluid should be examined after each course or each pair of courses. Not infrequently it will be found that the fluid has become normal after a few months' treatment. If so, the prognosis is good and treatment should be conducted along general lines. On the other hand, if the strength of the Wassermann reaction is the same or only slightly

altered after four to six months of intensive general treatment it may be well to resort to intraspinal therapy.

In tabes dorsalis, because of the apparent sensitiveness of many cases to mercury, it is better to start the treatment with small intravenous doses of salvarsan, gradually increasing and giving a treatment every week for a course of six or eight injections. If at the end of this course the Wassermann reaction in the fluid is considerably weaker, a course of mercury may be tried, followed by another course of salvarsan, alternate courses being given with periods of rest until the fluid is brought to normal. Many cases will be found, however, in which the strength of the reaction is only slightly altered by such a plan of treatment. The substitution of combined intraspinal and intravenous therapy in these patients will usually result in an improvement in the condition of the fluid. I am convinced that our aim should be to bring the fluids to normal and keep them there, if we intend to speak of a cure of the syphilis. That this can be done in a majority of instances is shown by Table III, which gives the results in thirty-seven cases followed for several years. All but three of these were tabetics, most of them well advanced. One was a case of diffuse myelitis, one of radiculitis, and one of ophthalmoplegia interna. The cases are arranged in groups according to the original strength of the Wassermann reactions in the fluid, and the last finding is indicated in the vertical columns. In thirty of the cases (81%), the reaction became negative with 1 cc. of fluid, but in two of these the reaction later increased in strength so that the final readings give twenty-eight (75%) negative. Nineteen of these cases are also negative with 2 cc., which is double the amount recommended by Hauptmann.[23] Of eighteen cases which were negative with 1 cc. or more, and have been followed from ten months to three and a half years without treatment, fourteen remain negative with 2 cc., two others remain negative with 1 cc. but positive with 2 cc. One relapsed to positive with 1 cc. and one with 0.6 cc. In those cases in which the Wassermann reaction of the fluid increased in strength, there was also a clinical relapse, while with a single exception in all the cases with persistent negative fluids, the disease has not progressed. In this one patient, who showed advanced tabes on admission, there has been an extension of the area of cutaneous anesthesia and a neuropathic arthropathy of the shoulder joint has developed, in spite of a normal fluid

TABLE III.—TABES DORSALIS. EFFECT OF TREATMENT ON WASSERMANN REACTION IN CEREBROSPINAL FLUID.

W. R. before treatment.	W. R. after treatment.								Amount of treatment. Before W. R. neg. with 1 c.c., or until stopped.			Between neg. with 1 c.c.; neg. with 2 c.c. or until stopped.		
	++++					−−	++++	−−	Mos.	Int. ven.	Int. sp.	Mos.	Int. ven.	Int. sp.
	0.2 c.c.	0.4	0.6	0.8	1.0	1.0	2.0	2.0						
0.2 c.c.		1←①		..	..	..	....	..	12	16	12			
0.2 c.c.		..	1	..	..	..	....	..	7	..	12 ns ss			
0.2 c.c.		..	..	..	1	..	....	..	24	32	15			
0.2 c.c.		..	..	..	..	1	....	..	1	..	4 ss			
0.2 c.c.		..	..	..	..	1	....	1	4	..	11 ss			
0.2 c.c.		..	..	..	..	1 —→		1	8	12	10	8	10	3
0.2 c.c.		..	..	..	..	1 —→		1	13	16	16	3	4	4
0.4 c.c.	....	1	..	..	..	..	....	..	6	..	13 ns			
0.4 c.c.	....	..	1	..	..	..	....	..	8	15	11			
0.4 c.c.	....	1 ←		①		..	....	..	5	..	12 ns			
0.4 c.c.	....	..	..	..	..	1 —→	1	..	11	21	7			
0.4 c.c.	....	..	..	..	..	1 —→	1	..	15	24	18	4	6	5
0.4 c.c.	....	..	..	..	..	1 —→		1	12	21	16	24	26	9
0.4 c.c.	....	..	..	..	..	1 —→		1	29	35	18	8	8	
0.4 c.c.	....	..	..	..	..	1	....	1	1½	3	2	cont.		
0.4 c.c.	....	..	..	..	..	1	....	1	12	14	11	cont.		
0.4 c.c.	....	..	..	..	..	1	....	1	17	14	29	cont.		
					←									
0.6 c.c.	....	..		..	1	①—]	①	..	6	11	8	8	13	1
				←										
0.6 c.c.	....	..		1		①—→		—①	..	..	..	8	17	17
0.6 c.c.	....	..		..	..	1	....	..	5	..	8 ss			
0.6 c.c.	....	..		..	..	1 —→	1	..	8	18	7	14	26	19
0.6 c.c.	....	..		..	..	1 —→	1	..	12	22	16	2	2	2
0.6 c.c.	....	..		..	..	1 —→		1	8	..	17 ns	9	17	16
0.6 c.c.	....	..		..	..	1 —→		1	4	6	5	6	9	9
0.6 c.c.	....	..		..	..	1	....	1	2	..	6 ns	4	8	
0.6 c.c.	....	..		..	..	1	....	1	5	8	6	11	21	
0.6 c.c.	....	..		..	..	1	....	1	4	7		11	20	10
0.8 c.c.	....	..	..		1	..	....	..	2	5	4			
0.8 c.c.	....	..	..		..	1	....	..	11	15	9			
0.8 c.c.	....	..	..		..	1	....	1	12(3)	20	5			
0.8 c.c.	....	..	..		..	1	....	1	3	6	6	cont.		
1.0 c.c.	....	..	..	..		1	....	..	1	2	2			
1.0 c.c.	....	..	..	..		1	....	..	1½	..	6 ss	cont.		
1.0 c.c.	....	..	..	..		1	....	1	1	2	2	cont.		
								→						
1.0 c.c.	....	..	..	..		1	①	—1	1	3	2	cont.		
1.0 c.c.	....	..	..	..		1	....	1	1	2	1	cont.		
1.0 c.c.	....	..	..	..		1	....	1	1½	..	6 ns			
37	....	1	3	2	3	28	4	19						
....	....	2.7%	8%	5.4%	8%	75%	....	49%						

① = relapse.
ns = normal serum alone.
ss = salvarsanized serum alone.

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and negative blood Wassermann reaction. It will also be seen that there is a certain correlation between the initial strength of the Wassermann reaction and the amount of treatment which was given before it became negative with 1 cc. The number of cases in some of the groups is too small for averages to be of value, but in general the 1 cc. or 0.8 cc. group required from one to three months, the 0.6 cc. groups about six months and the 0.4 cc. and 0.2 cc. groups about twelve months. Not infrequently an equal or greater amount

of treatment was required to change the reaction from negative with 1 cc. to negative with 2 cc.

In the presence of a rapidly advancing case of tabes or of optic atrophy where it is desirable to arrest the progress of the disease, in an important organ, the institution of combined intravenous and intraspinal therapy at the beginning should be seriously considered as rapidity of cure is the end to be accomplished.

TABLE IV.—PARALYTICA DEMENTIA. EFFECT OF TREATMENT ON WASSERMANN REACTION IN CEREBROSPINAL FLUID.

W. R. before treatment.	W. R. after treatment.							Amount of treatment.		
	++++					−	++++	Mos.	Int. ven.	Int. sp.
	0.1	0.2	0.4	0.6	1.0	1.0	2.0			
0.1 c.c.	1	....	....	....	....	....	....	23(6)	11	8
....	1	....	....	....	....	....	....	18	31	18
....		....	1	....	....	....	....	20	38	26
0.2 c.c.	....		....	1	....	....	....	14	24	24
0.4 c.c.	....	....		1←	—①	...	....	36(11)	25	21
0.6 c.c.	....	....	....	1←			—①	30	50	32

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Compared with the results in other forms of lues of the central nervous system, the treatment of paralytica dementia has been disappointing. With the proof of the active syphilitic nature of this disease, it was thought that a cure might be expected from intensive treatment, but there is something in the nature of the disease which apparently prevents the remedies from reaching the spirochete in sufficient quantities to eradicate them completely. It is true that most of the cases improve clinically and in some of them there is a marked improvement in the condition of the spinal fluid. Still, with corresponding amounts of treatment this response is much less marked than in tabes. In addition, there is a decided tendency for pleocytosis and Wassermann reaction to increase in intensity when treatment is discontinued. In two of our patients (see Table IV) there was at first almost as marked clinical improvement and diminution in abnormal elements in the cerebrospinal fluid as is seen in tabes. Both have had two relapses and with each relapse the response to treatment has been less marked. This indicates that as the paretic process grows older it is less amenable to treatment and probably explains the difference in results from state

hospitals for the care of the insane and those from private physicians. In state institutions the cases are usually much more advanced than those which come under the observation of private institutions or practitioners. Thus Runge[24] reports 37.4% remissions, Raecke[25] 55.4% improved, on salvarsan intravenously, Cotton[26] with combined intravenous and intraspinal therapy 68% arrested or much improved, and Ogilvie[27] 34% with complete remissions, and 40% incomplete remissions, a total of 74% improved. In four of Ogilvie's cases both the blood and spinal fluids were brought to normal. When we compare these results with the number of remissions in the pre-salvarsan era 5.7%[24] or 7.4%[28] the treatment of paretics seems justified. The return of a paretic to his business, even though it be for only six months or a year, is often of vital importance to his associates and family. Compared with our therapeutic effects in chronic cardiac or renal disease the results obtained thus far in paresis are decidedly encouraging, although in none of these diseases can we speak of a cure.

In the treatment of syphilis of the central nervous system we should never forget the patient, and that he may be suffering from disease of other vital organs. If there is marked ataxia, Fraenkel's reëducation movements are useful; if he is emaciated, attention should be directed towards diet and general nutrition. Most patients with this form of disease show a certain amount of mental abnormality. Here psychotherapy is of value. In other words, treatment must be individualized, and while a general plan should be followed in the various forms of the disease, each case may demand a certain deviation to meet the peculiar conditions.

The objects of therapy are threefold: first, the cure of disease; second, the amelioration of symptoms; third, the prolongation of life. With the possible exception of paresis, all of these objects may be attained in most cases of syphilis of the central nervous system. To be satisfied with the attainment of the last two without attempting to attain the first is to fail to apply all the means at our disposal.

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SYPHILIS AND SOCIETY.

HUGH CABOT, M.D.,

Boston, Massachusetts.

Assistant Professor of Genito-Urinary Surgery, Harvard Medical School, and Chief of Genito-Urinary Department, Massachusetts General Hospital.

Since the other papers in the discussion have concerned themselves with what syphilis does to society it may perhaps not be improper for me to consider what society does or may do to syphilis. As premises to this discussion we may admit that syphilis is the most serious of the contagious diseases which has not as yet been subjected to control. We may further admit that it is essentially a controllable disease, that in its early stages it is entirely curable, and that at all stages it is controllable as concerns its contagious nature, and that finally it seems likely that if Society should fail to control syphilis, Syphilis is not likely to fail to control society. Upon this basis we may proceed to consider what Society has done in attempting its control and then what Society may properly be expected to do in the immediate future.

Reporting of Cases to Public Health Authorities as a Measure of Control.

Eleven states, namely, California, Connecticut, Indiana, Iowa, Kansas, Louisiana, Michigan, Ohio, Utah, Vermont and Wisconsin have enacted laws or State Board Regulations looking to the reporting of cases of venereal disease in general and syphilis in particular. Seven cities, Cleveland, Detroit, Los Angeles, New York, Rochester, N. Y., Salt Lake City and San Diego have municipal regulations requiring the reporting of these conditions in some form. It thus appears that both state and municipal health authorities have regarded reporting of cases with favor, though the reckless manner in which legislation is enacted in this country may properly leave us in some doubt as to whether these laws were passed after due consideration or simply at the request of some enthusiastic ignoramus or in accordance with a thoroughly uninstructed and ignorant public outcry. However, reporting has been for many

years advocated as a method of reaching the disease and the probability of success is worth serious consideration.

At the outset of any attempt to estimate the value of reporting as a public health measure it is necessary to distinguish between true reporting and false reporting. True reporting requires that the case be notified to the health authorities by name and address precisely as are cases of other contagious diseases, including tuberculosis. False reporting is reporting by number or by some quasi-secret method and is evidently an attempt to deal with these conditions in a manner not thought applicable to other forms of contagious disease. On the question of value of reporting there are three main types of opinion:—

(1) The opinion of the public health officer.
(2) The opinion of the practising physician.
(3) The opinion of the enthusiastic layman (generally woman).

(1) Broadly speaking, the opinion of the public health officer has generally been in favor of reporting. In June, 1913, the annual conference of state and territorial public health authorities with the United States Public Health Service approved a model law for morbidity reports prepared by a committee of that conference. This law provided for the reporting of venereal disease, including gonococcus infection and syphilis, but in the section specifying how the reporting should be done there is inserted "Provided that in the reports of cases of venereal disease the name and address of the patient need not be given." It thus appears that though as a group they favor reportability they recognize the difficulties which stand in its way and are prepared to temporize with half-way measures. Such measures can only be justified on the ground that they represent a step towards true reporting and are intended to get public opinion accustomed to the appearance of these diseases in the weekly or monthly reports and later to support the attempt to make these diseases truly reportable. To this it may properly be objected that reporting by number not only has no statistical value but is positively misleading. There is no method of identification of the case and while it is to be presumed that a large number of cases will not be reported at all it is equally to be presumed that the same patients will be reported upon a variety of occasions by different physicians or institutions, this conclusion being justified by

our knowledge of the extremely peripatetic habits of these individuals.

(2) The opinion of the practising physician and particularly of those physicians who deal with syphilis on a large scale has been almost unanimously opposed to reporting. They reason that if physicians are required to report these patients by name they will in a short time, if they are honest, have no patients to report. This will have the exceedingly undesirable effect of throwing this disease into the care of the dishonest physician, the quack, and the charlatan, and, far from acting as a method of controlling the disease, it will not only make it less controllable but more severe in its manifestations. They further reason that if the reports are really private if made by name, they are of no practicable value to the health officer since by the very nature of his agreement with the patient he is stopped from using the information for the benefit of the public health, and finally they point out that if the report is made only by number no important statistical evidence will be obtained, duplication will certainly occur, and no benefit will result. That the latter argument is cogent seems to be borne out by the experience of New York city where physicians and institutions have been urged to report by number. From the reports of the month of November and December, 1915, and January, 1916, it appears that the number of cases of syphilis reported in a week varies from 564 to 195, and surprisingly enough, the number of cases of syphilis reported is almost double the number of cases of gonococcus infection during the same period, 4114 as against 2379. That there are doubtless a variety of perfectly good reasons for this extraordinary result may be admitted but it collides so violently with the facts and with common sense that it is impossible to regard such figures as having scientific or even social value.

(3) While it may be doubted whether it is worth while to introduce into this discussion lay opinion, it should be borne in mind that lay opinion has been an exceedingly important factor in placing legislation about these matters upon the statute books, and though we may properly believe that such opinion is rarely based upon a knowledge of facts that would entitle the individual to any opinion at all, we cannot disregard it as a factor in social activity. Average lay opinion appears to take the view that the prevalence of syphilis in the community is a shocking condition largely aided and abetted by the medical profession in their attempt to shield their

patients. There has been much agitation from women's clubs and associations, and particularly from the more boisterous advocates of woman's suffrage, most of whom regard the problem as a simple one and the remedy to lie in universal suffrage. Very generally, lay opinion has supported suggestions to make this disease reportable, and much existing legislation has come either from this source or from the advocacy of the public health officer with an amiable disregard of the gross improbability that such legislation will serve any useful purpose and the almost absolute certainty that it will only encumber the statute books with laws that are unenforcible and serve no purpose other than to bring the law into well-merited contempt.

After a pretty thorough study of this question of reporting I cannot avoid the opinion that it has been worthless as a method of assisting in the control of this particular variety of contagious disease. Public opinion has stamped syphilis as a shameful disease, as we all know without sufficient justification, and has therefore driven these unfortunate persons into hiding. From this hiding they have begun to emerge and are more and more seeking the advice of well trained honest physicians. From these physicians they expect and will receive protection since they have entered into an implied contract and one which cannot properly be disregarded. To the extent that the treatment of syphilis is in the hands of such practitioners, to exactly that extent the disease cannot be made reportable. Such portion of the cases as are in the hands of dishonest practitioners and charlatans are inaccessible to the law since these people will beat not only the law but the patient. Any law which is to achieve success must be of practical benefit to the patient, a fact which must have been commonly overlooked by the advocates of reportability. As generally proposed it is an attempt to protect the community against a contagious individual without any corresponding benefit to him and with a very large probability that it will do him considerable damage. Until such time as we are prepared to enact legislation which will be of at least as much benefit to the syphilitic as to the community, we may as well dismiss this kind of legislation as a factor in improving the situation.

Legislation Making Syphilis a Bar to Marriage.

Nine states, namely, Indiana, Michigan, North Dakota, Oregon, Pennsylvania, Utah, Vermont, Washington and Wisconsin, have

legislation which purports to make syphilis a bar to marriage, but in most of them the laws are such as to be largely worthless. Thus the enlightened legislature of Utah, Washington and North Dakota prohibits marriage of persons having syphilis except where the female is over forty-five, apparently having no interest whatever in the lady after that period. The Solons of Wisconsin and Oregon prohibit only the male, allowing the female to disseminate the disease at will. Utah and Michigan forbid the marriage but require no affidavit. Indiana, Pennsylvania and Washington require an affidavit and thereby put a premium on perjury. North Dakota, Oregon and Wisconsin require a medical certificate showing freedom from such disease. Those states which forbid the marriage of the syphilitic but require only an affidavit or nothing at all obviously cannot expect to diminish the number of such individuals who marry and these laws therefore in practise only enable the state to step in after the fact. Such laws while perhaps of interest in divorce preceedings cannot be regarded in any sense as public health measures. The states which require a medical certificate have undertaken a much more pretentious measure and it is of interest to look into this question in some detail. Wisconsin has the latest legislation on this subject and it may be taken as a type of present day legislative cerebration. It went into effect January 1, 1914. For the sake of completeness it is here reproduced in full:—

CHAPTER 738, LAWS OF 1913.

AN ACT.

To create section 2339m of the statutes, relating to marriage and venereal diseases.

The people of the State of Wisconsin, represented in Senate and Assembly, do enact as follows:

Section 1. There is added to the statutes a new section to read: Section 2339m. 1. All male persons making application for license to marry shall at any time within fifteen days prior to such application, be examined as to the existence or non-existence in such person of any venereal disease, and it shall be unlawful for the county clerk of any county to issue a license to marry to any person who fails to present and file with such county clerk a certificate setting forth that such person is free from acquired venereal diseases so nearly as can be determined by physical examination and by the application of the recognized clinical and laboratory tests of scientific search. Such certificate shall be made by a licensed physician, shall be filed with the application with the license to marry and shall read as follows, to wit:

I, (Name of physician).....being a legally licensed physician, do certify that I have this.....day of....., 19...., carefully and thoroughly examined, (Name of person)....., having applied the recognized clinical and laboratory tests of scientific search and find him to be free from all venereal diseases so nearly as can be determined.

.....Signature of physician.

2. Such examiners shall be physicians duly licensed to practice in this state, shall be persons of good moral character and of scientific attainments and at least 30 years of age. The fee for such examination, to be paid by the applicant for examination before the certificate shall be granted, shall not exceed $3.00. The county physician of any county shall, upon request, make the necessary examination and issue such certificate, if the same can properly be issued without charge to the applicant, if said applicant be indigent.

3. Whenever there is a dispute or a disagreement regarding the findings of any medical examiner, laboratory tests shall be made in the State Laboratory of Hygiene from material submitted by such examiner, and the findings of said laboratory shall be accepted as evidence of the presence or absence in the person examined of any venereal disease.

4. In any case wherein the certificate of health required by subsection 1 of this section shall be refused and the applicant shall make and file with the county clerk of the proper county an affidavit setting forth the fact that such applicant has not had a fair and impartial examination, and that he is entitled to such certificate of health, it shall be the duty of such county clerk to certify such proceedings, at once, to the county court of such county without formality or expense to such applicant. Such application shall be heard by a judge of said court, at the earliest time practicable, without a jury in court or in chambers during the term or in vacation as the case may be. Notice of the time and place of such hearing shall be given to such applicant by mail. A certified copy of an order of such judge upon his findings in such matter determining that such applicant is entitled to such certificate of health presented and filed with such county clerk shall have the same force and effect as such certificate and such county clerk shall thereupon issue a license to marry, to such applicant.

5. Any person a resident of this state, who with intent to evade the provisions of this act shall go into another state and there have a marriage solemnized and who within one year from date of such marriage shall return and reside in this state, shall upon information or knowledge to the district attorney of any county be required by him to file with the county clerk of any county in which such person may be then a resident, a certificate of examination from such physician as set forth in this section. Any person violating the provisions of this subsection shall be punished by imprisonment in the county jail not less than thirty days nor more than one year.

6. Any county clerk who shall unlawfully issue a license to marry to any person who fails to present and file the certificate provided by subsection 1

of this section, or any party or parties having knowledge of any matter relating or pertaining to the examination of any applicant for license to marry, who shall disclose the same, or any portion thereof, except as may be required by law, shall upon proof thereof be guilty of a felony, and shall be punished by imprisonment in the state prison not less than one year nor more than five years.

7. Any person who shall knowingly and wilfully make any false statement in the certificate provided for in subsection 1 of this section shall be guilty of perjury and upon conviction shall be punished as for perjury, and a conviction under this subsection shall revoke the license of such physician to practice in this state.

Section 2. All acts or parts of acts inconsistent with the provisions of this act are repealed.

Section 3. This act shall take effect on and after January 1, 1914. (Approved August 1, 1913.)

Between the time of its passage and the time at which it went into effect it was duly pointed out that if the law meant what it said, it would require of physicians an amount of time, knowledge and scientific equipment entirely out of proportion to the fee required by law. This difficulty the State Attorney General was asked to untangle and this he did in an opinion rendered December 22, 1913, which reads in part as follows:

"If there are clinical and laboratory tests, such as the Wassermann test, which require special study and special apparatus for their application and which only a very small per cent. of the licensed physicians of scientific attainments can apply, I am convinced that the law was not intended to require and therefore does not require such tests. I do believe that the law was enacted on the assumption that physicians, more than any other class of citizens, would appreciate the wisdom and necessity therefor and would co-operate to the best of their ability in its enforcement. The purpose was not to provide a new source of revenue for the doctors; nor, on the other hand, was there an intent to place an undue burden on them. No doubt reliance was placed on the well-known public spirit of the medical profession and the fee fixed at a figure which would cause hardship neither to the applicant nor to the examiner. It is, of course, apparent that physicians can be found who will issue the required certificates no matter what tests the law may be deemed to require, so that unless the reputable physicians will co-operate to make the law effective (and if they will not, no law of the kind can be successful) the law must largely fail to accomplish any good. But I am convinced that the great mass of reputable physicians will desire to save the law and the profession from disrepute, and will therefore endeavor to carry out the spirit of the enactment and hold themselves ready to give such examinations and tests as the ordinary reputable physician of scientific attainments is equipped to make and may reasonably be expected to make for the fee prescribed. Otherwise it is plain that the charlatan of the profession will seize on this law as a new source of revenue and thus

bring the law into disrepute and dishonor to their profession. I am of the opinion that the law must be given a practicable and workable construction, rather than one that will defeat its purpose and possibly render it unconstitutional and void; that its obvious purpose was to require only such an examination and test as the ordinary reputable licensed physician of scientific attainments is equipped to make, is capable of making, and could reasonably be expected to make for the fee of $3.00, and that the 'recognized clinical and laboratory tests of scientific search' do not include the so-called Wassermann tests, nor such tests as can be made only by specialists, nor such as require special and expensive equipment or long laboratory experiments."

In discussing the effect of this legislation in February, 1914, the health officer of the state of Wisconsin made the following remarks:

"If the action of the legislature reflects public opinion, and in Wisconsin we believe it does, then the public is strongly in favor of a provision similar to this, as the vote of the members of the legislature was almost unanimous in favor of the measure. Also very little dissention or unfavorable opinion on this law is heard from the general public, the controversy, as before stated, originating almost entirely on the part of physicians. Neither do the male applicants for marriage materially object to the provisions required, but on the contrary, my personal experience has been that all such applicants are strongly in accord with the provision of the law. Whether the law will stand the test of the supreme court or not cannot be foreseen. One of the great benefits to be derived from any law is the education of the public. That the controversy concerning this law has awakened a great interest and set the people of our state thinking cannot be questioned. The good effects, therefore, whether the law is to remain upon the statute books or not, will be extremely beneficial and far reaching, not only in Wisconsin, but in adjoining states which have become interested in the experiment."

That legislation of this sort interpreted by such judicial opinion and backed by such public health authorities can exist in a civilized community to-day is the most discouraging feature of the attempt to control syphilis. One need not be surprised that the legislature, confused by a mass of undigested requests that "Somebody do something," overwhelmed by medical technicalities of which it had but the slightest comprehension, should have passed such a law, nor need one be astounded that an attorney general in the praiseworthy desire to keep in the good graces of the electorate should support by his opinion so ridiculous an enactment, but it is indeed discouraging to find the public health officer of the State lending comfort to the enemies of progress in such a manner. Let us for the moment take the most favorable view of such a law. If the physicians honestly try to live up to the opinion of their attorney general, less than one in a hundred could, by any stretch of imagination, be

regarded as competent to give an opinion if he had before him all the evidence. If such medical men were willing to support their opinions by the painstaking collection of the evidence they would of necessity be contributing to the state thousands of dollars not only in time but in actual cash which they must pay for the proper laboratory investigations. This would in effect single out the physician for another special form of taxation. If being honest, but careless-minded, they were willing to give an opinion without all the evidence they would be making themselves parties to the most dangerous kind of guesswork calculated to do nothing but place a legal sanction upon the transmission of disease. Since it is unthinkable that these certificates will be given only by the competent who are willing to pay handsomely for the privilege of giving such certificates, it therefore follows that the state of Wisconsin has, through its legislature, backed by its attorney general, with the sanction of its public health officer, engaged in the business of licensing the marriage of syphilitics.

MARRIAGE.

Amendment to the Law Requiring Physical Examination of Male Applicants for Marriage License. (Chap. 525, Act August 10, 1915).[1]

Section 1. Subsections 3, 4, and 5 of section 2339m of the statutes are hereby repealed.

Sec. 2. Subsections 1, 2, 6, and 7 of section 2339m of the statutes are amended to read:

Sec. 2339m. 1. All male persons making application for license to marry shall at any time within 15 days prior to such application be examined as to the existence or nonexistence in such person of any venereal disease, and it shall be unlawful for the county clerk of any county to issue a license to marry to any person who fails to present and file with such county clerk a certificate setting forth that such person is free from venereal diseases so nearly as can be determined by a thorough examination and by the application of the recognized clinical and laboratory tests of scientific search, when, in the discretion of the examining physician, such clinical and laboratory tests are necessary. When a microscopical examination for gonococci is required, such examination shall, upon the request of any physician in the State, be made by the State laboratory of hygiene free of charge.

The Wassermann test for syphilis when required shall, upon application, be made by the Psychiatric Institute at Mendota free of charge. Such certificate shall be made by a licensed physician, shall be filed with the application for license to marry, and shall read as follows, to wit:

[1] I have not overlooked this amendment, the effect of which seems to me to render confusion worse confounded.—H. C.

I, (name of physician), being a legally licensed physician, do certify that I have this.....day of.....19...., made a thorough examination of (name of person) and believe him to be free from all venereal diseases.

.....
(Signature of physician.)

2. Such examiners shall be physicians duly licensed to practice in this State. The fee for such examination, to be paid by the applicant for examination before the certificate shall be granted, shall not exceed $2.00. The county or asylum physician of any county shall, upon request, make the necessary examination and issue such certificate, if the same can be properly issued, without charge to the applicant, if said applicant be indigent.

3. Any county clerk who shall unlawfully issue a license to marry to any person who fails to present and file the certificate provided by subsection 1 of this section, or any party or parties having knowledge of any matter relating or pertaining to the examination of any applicant for license to marry, who shall disclose the same, or any portion thereof, except as may be required by law, shall upon proof thereof be punished by a fine of not more than $100 or by imprisonment not more than six months.

4. Any physician who shall knowingly and willfully make any false statement in the certificate provided for in subsection 1 of this section shall be punished by a fine of not more than $100 or by imprisonment not more than six months.

To sum up now the question of the benefit derivable by reporting cases of syphilis to the public health authorities and the requiring of certificates for marriage, my opinion is this: In the present state of public opinion the reporting of syphilis can have no scientific value in the production of statistics and can have no medical value in the control of the disease. If it be suggested that pseudo-reporting is of value in the instruction of the public, we may properly inquire in what this instruction consists. If it is supposed to spread information in regard to the prevalence of the disease, it must be pointed out that such information is contrary to the fact and misleading. If it is suggested that it is of value as a purely educational measure, we must reply that as an educational campaign it is a failure, and that if the same amount of time, effort and money were spent upon a real campaign of education far better results would be obtained. In regard to the issuance of marriage certificates under any machinery now required by the law, I am strongly of the opinion that any benefit which may result is more than counterbalanced by the harm. It must be obvious to any observer familiar with the intricacies of the diagnosis of syphilis that it is

extremely difficult to deny the presence of the disease at any given time, particularly if the antecedents and previous history of the patient are unknown. The probability of error becomes almost overwhelming if there is any lack of co-operation between the physician and patient. Keyes has pungently pointed out that the diagnosis of the presence of syphilis at any given moment may be a matter of supreme difficulty. He has shown that the symptoms are of little value, that the Wassermann reaction is of value only when taken in connection with an exhaustive knowledge of the previous history, that it may be negative in the active stages of the disease, that it may be artificially made negative for the purpose of examination, and that it may well be positive in individuals whom all of us believe to be permanently free from the possibilities of conveying their infection. Thus the harm which such legislation as that above referred to may do consists in a false sense on the part of the legislature that it has done something for the benefit of the community, and on the part of the public that its health officers are engaged in stamping out the disease. It gives rise, in a word, to a false sense of security, protects the unscrupulous, penalizes the honest, and deceives the community in general by what can only be described properly as fake certificates.

Though it appears to me to be abundantly clear that legislation is not likely to be of assistance in preventing the marriage of syphilitics, no doubt can exist that there is a very real demand on the part of society for the prevention of such a possibility. It therefore follows that it is of the first importance that existing medical opinion as to what constitutes freedom from danger of infection for the purposes of marriage should be authoritatively stated. There is at the present time difference of opinion between those who may be properly regarded as authorities, to such an extent as to be confusing to physicians and confounding to the public. For instance a very considerable body of first class opinion holds that marriage may be allowed at such time as it appears that the possibility of transmitting the infection to wife or children is at an end. Opposed to this is a somewhat smaller body of opinion, but of equally eminent qualification, which holds that the possibility of the development of the late manifestations in the central nervous system make the individual socially unsound, and should therefore be regarded as a bar to marriage. Of course, if this view should prevail, it would be equally imperative to forbid marriage between patients with

cardiac disease, chronic nephritis, and a great variety of other ailments which make them notably more unsound than does the somewhat shadowy prospect of tabes or paresis. In view of this wide divergence of opinion and widespread and wholly intelligent demand for a clear statement of what should be regarded as conditions operating as a bar to marriage, I believe that this Congress can do an important service by formulating expert opinion in concrete form, and I would therefore suggest to the properly constituted authorities of this Congress that, if in their opinion it is advisable, a committee be appointed to make report on this subject.

What Society Does for the Individual in the Way of Diagnosis and Treatment.

I have thus far considered only what Society has attempted to do through the medium of legislation and have felt obliged to conclude that such measures as it has undertaken are substantially worthless if nothing worse. It is next interesting to inquire what steps Society in general has taken to advance the interests of the individual with syphilis and to this extent and in this way make up for the harm which it has done him by imposing or attempting to impose burdens upon him. In attempting to estimate what the state or municipality may properly undertake to do in regard to the diagnosis and treatment of syphilis one looks around in vain for any other disease of like importance with which it can be compared. Our attempt to segregate and control tuberculosis is perhaps the most nearly comparable, but we get little assistance from this comparison because of the peculiarly subtle way in which syphilis is a menace to the public health. The victim of tuberculosis himself may under certain conditions be a considerable source of danger to others but he can never transmit his disease to another generation and in this way undermine the constitution of the nation. Furthermore the victim of syphilis is far more illusive—a condition for which we have ourselves largely to blame. That the numerical side of the proposition is somewhat similar to tuberculosis many believe, but such estimates are based upon the merest guesswork and we seem unlikely to get reliable figures for a long time to come.

Society has been singularly backward in making proper provision for this condition and even at the present time only the very beginnings of proper arrangements are to be found. In regard to diagnosis, six states, and perhaps others, are prepared to assist phy-

sicians, namely, California, Connecticut, Massachusetts, Vermont, Washington, and Wisconsin, but a number of cities scattered over the country have taken the matter up and are more or less well equipped to do a Wassermann reaction. I cannot find that there is any state which has made important provision for the treatment of venereal disease and though Massachusetts is favorably quoted in this regard such provision as there is exists only in the state almshouse and in the prisons. Various cities, notably New York, Cincinnati, Detroit, Buffalo, Cleveland, Philadelphia, Newark, Rochester, N. Y., and St. Louis have made provision for hospital treatment but at best on an inadequate scale. To my mind the most interesting attempt in this direction is that made by the University of Michigan in its hospital at Ann Arbor under the direction of Professor Wile. Here at least a real beginning has been made—accommodations generous as compared with most other hospitals, equipment of high order, and first class professional skill have been collected together. It shows ample results in the way of reaction from the community to justify the belief that it is but the beginning of such a method of dealing with syphilis and it may well serve as a model for other communities and institutions.

While it must be freely admitted that such a showing as this of state, municipal, and hospital care has not begun to scratch the surface of the problem, there can be no doubt that this is the line along which progress must be made and is our chief hope for bringing syphilis under control. While in this country public opinion is as yet quite blind to the requirements, it cannot be regarded as seriously experimental. The Scandinavian countries have undertaken the wholesale treatment of venereal disease as a public undertaking and, though much difference of opinion exists in regard to the details, I have heard of none in regard to the principle. Here, therefore, lies the most fruitful field of effort. The state, the municipality, and the university or corporation hospital must prepare to deal with syphilis upon a large scale not only in regard to diagnosis but in regard to treatment and subsequent supervision. Doubtless the reason which has blocked most attempts in this direction has been the size of the problem and the belief that the cost would be overwhelming. It is probably the cost rather than the size which has given us pause and yet in regard to cost I believe we have been altogether too easily frightened. It has been assumed that treatment should be free or partly free and that the whole burden of the

expense must come upon the tax payer, who has naturally shied at the prospect. Here seems to me to lie the error. Untold millions are to-day spent by individuals in a more or less futile attempt to be properly treated, much of this going into the pockets of quacks and charlatans with no benefit whatever to the community. Under proper management the whole of this can be swung into the coffers of the state or hospital. There is no reason why Society should fear to step in to separate the patient from the private physician. The management of syphilis by the private practitioner has fallen far short of reasonable success, in large part because the interests of the community can in no way be safeguarded. If public or quasi-public institutions should offer as part of their hospital system thoroughly competent treatment of syphilis it can hardly be doubted that the public in general would at once take advantage of such an offer. Diagnosis and treatment alike for all should be offered at a sliding scale of fees proportionate to the wages or salary of the individual. A full-time salaried staff should be put in charge and these salaries should be made sufficient to attract first-class professional ability. As soon as it became widely known that such services were to be had in general hospitals where no stigma could attach to the patient, the charlatan would be ruined, many incompetent physicians would lose a large part of their work, and some eminent consultants would be at the service of the state. While managed in this way the numerical size of the problem would probably be large, and while it would probably require for its beginning considerable expenditure by the state or by private institutions to provide sufficient equipment and sufficient scientific staff, I am strongly of the opinion that it would be or would become a highly profitable investment, paying dividends not only in cash but in a better population. The greatest difficulty which is likely to arise in the course of this attempt will be the lack of control which such institutions would have over their patients. It is arguable that it would be desirable to have legislation empowering certain institutions as deputies of the state to compel the attendance of patients during such periods as seem desirable. I believe that such legislation would not seriously invade the proper rights of the individual and would therefore not meet with violent opposition. Should such a system become widespread, we should then have a comparatively accurate view of the size of the problem and of the probability of being able to bring syphilis within the fold of curable diseases.

At such a time when the state was not only prepared but had shown its willingness and ability to care for its citizens, then, and then only, should we again return to the discussion of reportability. We may properly admit that the individual has no rights which the public is bound to respect to its own disadvantage, but if we are prepared to ride roughshod over the rights of the individual we must also be prepared to show not only advantage to the state but justice to him whose rights we have sacrificed for what we judge to be corresponding benefits for the whole. In a democracy, certainly, justice must be reasonable, unenforcible laws must be avoided, legislation must follow and not precede average sound public opinion.

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Discussion.

Dr. Isadore Dyer (New Orleans): A wide range for discussion is offered in the topics which have been so ably presented, but it would be difficult to engage all of them with any hope of adding much to the material furnished. With the idea of furthering the sociological feature of the program, some ideas might be presented which may have been overlooked.

In weighing the question of syphilis in its relation to society, meaning in the social economy of all people, there are two points which seem to stand out, the lack of control of syphilis and the effect this has upon those who have not voluntarily contributed to its spread, namely those who may have acquired syphilis innocently and those who have escaped it.

Almost the entire attention of those who work with syphilis and of those who write on syphilis has been devoted to the care and

cure of syphilis; little has been actually accomplished in its control and in its prevention. We may admit that certain eugenic laws have been passed and promulgated with a view to disciplining those who have contracted the disease and such laws may ultimately have their effect in protecting the children in some future generation, but the enforcement of these laws is going to be difficult and it is not hard to calculate that many will escape by one or another means.

The treatment of syphilis has improved enormously in recent years and the ability to make exact diagnosis has added materially to the possibilities of cure. Notwithstanding, the attack upon the sources of the disease has not yet been undertaken with sufficient force.

In a review of a large number of general hospitals, it was ascertained by the writer that practically all of them refused admission to early or incipient cases of syphilis, that the ambulant case was generally not wanted in the hospital and that all cases of syphilis, as such, were accepted on sufferance. The outdoor clinics everywhere show a great preponderance over the cases of syphilis in indoor services and, where any statistics could be had, the clinics handle early syphilis almost always without the proper consideration of their danger to the community.

In spite of these facts, there are many hospitals which practice routine Wassermann tests for one or another reason, but apparently without any purpose directed at the control or prevention of the disease, so far as the early cases are concerned.

It can be stated as a very safe hypothesis that if every case of syphilis with a chancre or with an early eruption could be promptly hospitalized and treated under compulsion, the disease could be controlled far better than through any system of legislation regulating the report of cases or determining the eligibility of such for marriage.

If enough of those who deal with syphilis could reach this point of view, it is rather certain that the hospitals would help, for in the large majority of hospitals approached on this question, the very emphatic opinion was derived that the authorities considered the hospitalization of all syphilitics desirable.

There has been a consistent objection on the part of general hospitals to receive incipient cases, some institutions going so far as to exclude such with other acute communicable diseases. If syphilis is to be controlled, however, this viewpoint must change,

for a provision for such cases in all general hospitals would offer the most potent means for the control of syphilis. Almost every physician attached to a venereal clinic could accomplish far more in the treatment of syphilis if all early cases were under prompt control.

Private patients with syphilis are more amenable to treatment and advice than those in public practice, but the latter need more regulation.

This phase of the discussion might be dismissed with the formulated propositions:

1° All general hospitals should have special provisions for the indoor care of incipient or acute syphilis and all men who treat syphilis in public practice should encourage the enforced indoor care of such patients with the object of getting these subjects under prompt control and thereby to minimize the spread of the disease.

2° Legislation should be directed at enforcing the hospitalization of all cases of acute syphilis coming under public charge.

3° Educational movement should encourage the public to recognize syphilis among the communicable diseases, and amenable to isolation just as are scarlet fever, measles, and other contagious diseases.

The hospital control of syphilis and the methods of diagnosis and care are closely related and no better means could be had of determining the best procedures, than with the continued observation of cases constantly under care.

There is another feature of note in considering a more general hospital provision and care for syphilis and that is the educational side.

The discovery and wide use of the newer arsenical preparations in the treatment of syphilis has placed in the hands of the medical profession a group of powerful remedies with rather exact relation to the disease. There has not yet elapsed time enough to fix the value of these preparations and yet the majority of the medical profession has grown to depend upon them in the treatment of the disease.

Former ignorance and timidity in treating syphilis have given place to a degree of rash use of these remedies which has not been wholly justified. Safely first is set aside for a cocksure confidence—often without proper estimate of the end results.

The medical schools are not teaching syphilis adequately. Most of them confess this in the general discussion which has taken place in the past few years as to how and by whom syphilis should be taught. Most medical colleges leave the instruction to the different faculties as the subject may apply and there are, as yet, few schools which syphilis is undertaken as a specific and essential subject.

All the more reason that the student and the physician should have the chance to study the disease at first hand among cases assembled in hospital wards under the direction of men qualified to teach the subject. The accidental or occasional obscure care of syphilis in a general ward offers little; and the transient case in the clinic affords only the casual observation of the disease, certainly not the exact study.

It is too early to argue for special hospitals for syphilis, for the public is not educated enough to see this necessity. This may come as the outgrowth of a more liberal provision in the general hospital and after the demand for accommodation of such patients will make a separate institution mandatory.

The social side of syphilis has many divisions—the study of the relation of syphilis to the economics of the state would lead us into a number of bypaths, including the tax laid by this disease upon the public in the asylums and in the prisons.

The present diagnostic methods which so readily determine exact cases and which clear up the obscure phases of syphilis have already established the widespread and hitherto uncalculated hereditary types of the disease, many times wholly unsuspected.

It is here that the argument for syphilis prevention has its greatest force. The subject of syphilis in the innocent is not sufficiently stressed in the usual discussion. This question ramifies into industrial life, social organization and involves the community as well as the home. The delinquent school child, or the defective worker of more mature years, may owe the continued obliquity to an unknown antecedent source of this character.

The responsibility of one case of innocent syphilis would be great; multiply such cases and the possibilities grow.

The enforcement of any law regulating the reporting of venereal diseases and especially syphilis will be difficult until there is some

beginning with such reports from hospitals which receive such cases and which treat them in indoor or outdoor services. As a rule, a record is made of these cases and these records are available by the hospital authorities who can make the proper returns at regular periods. In time such records may serve a useful purpose in checking up the spread of syphilis.

The report of cases of syphilis in private practice will require more education, of both the profession and the laity. The provisions for the regulation of marriage through forbidding syphilitics the license to engage such a contract have been so far the result of a ferment among health officials of mixed minds. The whole business is of doubtful efficacy, so long as the law is so arbitrary as at present. The strong conviction among the framers of such laws seems to be that syphilis is an incurable disease.

Gonorrhea is brought under the same ban as syphilis because it is vicious. Dr. Cabot has very properly argued that any such legislation should be generally directed at disqualifying the unfit and that any physical condition, whether due to syphilis, tuberculosis, insanity, or to any other cause should be considered.

The regulation of such eugenic propositions must bring the full force of the police powers of state health authorities to bear, before any actual results can be anticipated.

The State Health Boards have become advisers as well as protectors in sanitary matters. After all, the prevention of marriages among the unfit is only one phase of social hygiene.

If the medical authority in each state were given the right to supply health certificates, covering particularly the diseases which disqualify for marriage, then it would be an easy matter for the State Board of Health, through its medical and laboratory forces, to dispense such certificates after a thorough review of the applicant, including all laboratory tests essential to a proper examination.

Such a method would do away with the objections made by the profession, now so critical of those laws which fix the fee for examinations to determine syphilis.

The State Board not only has the equipment for such examinations, but it has some obligation at the same time.

At this time certain State Boards already offer their laboratories for the proper examination of pathological specimens; in many states, the health body makes it compulsory to have examinations made for diphtheria, typhoid, etc.

The additional advantage of a central bureau of record of all such persons as have had a board examination would make for a more systematic knowledge of the incidence of such diseases, and of syphilis especially.

To leave the certification of the condition of a supposed syphilitic to the average physician, upon his own examination, would soon nullify any law, for no system of report could be assured, and no standard test could be enforced.

If state legislation regulating marriage required that all individuals party to such contract, whether man or woman, should file a certificate of the State Board of Health, declaring his or her state of health, and if such legislation provided that the unfit could not be licensed to marry, then syphilitics among other unfit could be barred.

The moral effect of such laws is the greatest after all, for the knowledge of such a requirement would have an early influence in deterring those who might contract diseases, such as syphilis, and it would prevent many who are cognizant that they have or have had syphilis from attempting marriage. The public record of persons with such diseases, too, would largely influence those with disease against marriage. In these respects, such legislation would be of large value in the way of prevention.

We are all apt to be hesitant over too radical a step in the regulation or control of syphilis, because, in the field of preventive medicine, to select one disease among a number which menace society is not truly scientific. The excuse we offer to ourselves is that syphilis is different because it is usually vicious and, more than that, the very nature of its occurrence under conditions of venereal indulgence has occasioned its spread without the same means of control which might apply to diseases of more innocent origin. The obligation rests upon the medical profession, for with it lies the means of prevention. Until now, the physician has taken no part in the moral or sociologic phases of syphilis. He has simply taken the point of view that his duty lay rather in remedying the physical side where he could and he has left the rest to the patient, to whom the moral question has seldom appealed.

The natural demand of the public has come—for the better protection of the future generations.

We may go on devising improved methods of diagnosis and of treatment and cure, and there will probably always be need for such devices. For some years to come we will need to provide for the derelicts in the wake of syphilitic invasion as found among our more and more refined civilization, but the time has come when the control of the incidence and spread of syphilis must be undertaken for the sake of the home and the community as represented by the economical phases of social and industrial life. The generally credited twenty to twenty-five per cent. morbidity from syphilis in the United States is a grave charge against our morality.

Dr. Hugh C. Patrick (Chicago): I am sure that first of all you will wish me to express our admiration for and gratitude to pioneers and research workers like Dr. Swift who have devised new methods of combating disease, and practitioners like Dr. Fordyce who have followed the pioneers to test their new methods in the crucible of practical experience, and men like Dr. Cabot who have made a well-balanced attempt to study disease in its relation to the social cosmos.

Regarding the question under consideration, I feel quite sure there are many in this room more competent to discuss it than I, but the pleasing naiveté of Dr. Swift and Dr. Fordyce in asseverating some long known facts regarding syphilis of the nervous system, encourages me to present a few hackneyed ideas on treatment. I entirely agree that in most cases success depends upon early, intensive and individual treatment, but we might ask what treatment fulfils these requirements. For the time being excluding tabes and general paresis, I should say that in the great majority of cases mercury and iodides fulfil these requirements *provided enough is given.* What is enough? Certainly not any given dose but enough to eradicate the disease or the limit of tolerance of the patient. Very frequently not enough is given, even by excellent practitioners. The statement has been made that after years of treatment by mercury and iodide beautiful results may be attained by the use of salvarsan. Equally I can say that after prolonged use of mercury and iodide with little or no effect, beautiful results are sometimes attained by the same remedies in really full doses. I beg the audience to pardon me for such elementary statements but I wish to note that in the majority of cases a man can take two huge

inunctions a day, provided the mouth is kept immaculate. And this does not mean the use of any "mouth wash" but the vigorous, thorough use three times a day of a *good* tooth powder, after a competent dentist has put things in order. And I venture to suggest that quite the best tooth powder I have found is powdered potassium chlorate cautiously (it is explosive) rubbed up with oil of cloves.

When it is important to get a quick effect, when there seems to be imminent danger, it is well to start with salvarsan (or neosalvarsan or arseno-benzol) as it acts more rapidly.

Another long-known fact that should be kept in mind is that iodides are in no sense spirocheticidal. They are of no use in treatment of the *disease*. Mercury and salvarsan are spirocheticides, are the remedies for the *disease* and have less effect upon the *lesion*. Iodides attack the lesion, the granulomatous tissue, the gumma, which is the result of the disease. It is this lesion in vessel or membrane which causes pain, paralysis, spasm or death. Furthermore, by attacking this gummatous tissue the iodides set free and make accessible to mercury and salvarsan the spirochetae embedded in it. In tabes and paresis there is none of this gummatous tissue and consequently iodide is of little use. Experience has shown that in some cases salvarsan is more effective than mercury, in others mercury is more effective and in still others alternation of these two remedies accomplishes most. Incidentally, I beg to enter a protest against the wave of arsenical mania which seems to have swept pretty well over this country. Why syphilis should be treated with cacodylate of soda when so much more effective remedies are at hand, is more than I can understand.

To dogmatize on account of limited time, I should say that in cerebro-spinal syphilis (tabes and paresis excluded) intra-spinal injections are rarely if ever indicated. Everything that can be accomplished can be attained by the other simpler and less hazardous methods.

Again to dogmatize, even with intensive treatment by the best and latest methods we do not know when the patient is really cured. I am ready to agree that a man with Wassermann free blood and spinal fluid for a year may be allowed to marry but that is not to say that he is cured for the rest of his life.

And now as regards tabes and paresis and the use of intraspinal injections. My limited time will allow no discussion of these

matters and so I shall only very summarily state what seem to me to be reasonable conclusions such as the facts up to date allow.

1. Tabes and paresis are syphilis of the central nervous system but they are syphilis with a difference or differences. Neither pathologically nor histologically nor clinically are they comparable to cerebro-spinal syphilis.

2. For these diseases salvarsan is probably more effective than mercury.

3. It has not yet been shown that in the majority of cases intraspinous injections are more effective than intravenous.

4. It is likely that occasionally the intraspinal treatment is more effective.

5. The indiscriminate use of intraspinal injections is to be deprecated. They should be administered only by trained men and after very careful diagnosis. Of all the methods used and proposed, that of Swift-Ellis is the least hazardous and is as efficacious as any but it is not devoid of danger.

Dr. Abner Post (Boston): It is not an easy task to discuss papers so full and so advanced. This congress is remarkable for the fact that the subject discussed to-day is the only subject that has been brought before the general meeting a second time. In 1891, at the Second Congress, of which Dr. Wier Mitchell was President, Late Syphilis was the subject for general discussion. Two papers were read. The first was a general résumé of our then knowledge, while the second was more concerned with hereditary syphilis. It drew attention to the fact that syphilis was seldom discovered in the autopsy room and made a plea for the more careful study of syphilis in the future, both clinically and in the laboratory, for its own sake and also because of its close relationship with all pathology. That such study has been done, the papers to-day have shown. Twenty-five years ago, there was no mention of spirochetes; the Wassermann test was unknown; Ehrlich had not given us his wonderful gift and intradural medication was undreamed of.

The burden of syphilis upon the community has been spoken of to-day. The burden upon the individual must be considered as a part of the burden upon the state. One need not look far to find syphilitic children left as a responsibility to their grandparents;

the brother or sister of the syphilitic parents caring for a syphilitic nephew or niece, or strangest of all, to find the second husband or wife assuming the responsibility for syphilis and syphilitic children of the first marriage. The burden is greater and greater the further we study it.

The disease is gaining a most important place in our nosology. It is being recognized as a disease and not simply as the evidence of a breach of morality. Pathologically, it is absolutely different from gonorrhea, with which it is sometimes associated and from which it is not yet entirely differentiated in our classification.

To brand it as always a disgrace, as we have done, is to put a premium on concealment and deceit. There is nothing in medicine which so encourages the existence of charlatans and irregular practitioners as the stigma put upon syphilis, no matter what its origin. The cases that should be classed as venereal are less than the majority. The accidental inoculations, the conjugal syphilis and the hereditary syphilis together far outnumber the venereal cases. One of our most honored members has suggested the possibility of other, as yet unrecognized, methods of inoculation.

Many hospitals are still unwilling to receive cases of syphilis as such and there must be very few men in this audience who have not helped to procure the admission of cases of syphilis to some hospital under some sort of subterfuge, and the disease has been entered on the hospital records as rheumatism or something which it is not. Not only are the hospital records falsified by the failure to record syphilis under its proper name, but the cases of syphilis are grouped under the name of some other disease and the records further falsified by the enumeration of these cases under headings where they do not belong. What are hospital records worth under such circumstances?

A similar condition obtains in death returns. The number of deaths which should be returned as due to acquired syphilis is probably small, but the number of deaths from hereditary syphilis is large. Those that we find in death reports come from the Almshouses. Deaths from hereditary syphilis in private practice are seldom reported as such. It is a brave physician who signs a death certificate to the effect that death has occurred from hereditary syphilis. Marasmus has been a convenient synonym, but that has been taken from us. Within a little while, a death certificate for a pair of syphilitic twins who lived less than twenty-four hours gave

cholera infantum as the cause of death and gas poisoning was the return in another case of heredo-syphilis. What are vital statistics worth under such circumstances?

The effect upon our profession of practicing such deceit must certainly be deleterious. The sooner we consider syphilis as a communicable disease and have it so recognized in hospital and death reports, the better.

This is not a plea in behalf of irregular living; it is a plea for justice to the innocent, for Christian charity and, above all, for scientific accuracy.

Dr. William G. Spiller (Philadelphia): I am not an advocate of intraspinous treatment of syphilis, at least not as the method of choice for beginning the treatment. I have seen excellent results obtained by other methods, provided, as Dr. Fordyce and Dr. Patrick have emphasized, the treatment was begun at an early stage of the disease and used persistently. It is impossible to obtain good results when destruction of nerve cells and nerve fibers has occurred, and the most that can be hoped for under such circumstances is arrest of the process. I prefer to begin with one-half the so-called full dose of salvarsan intravenously in association with the salicylate of mercury given intramuscularly, and have obtained most satisfactory results in many early cases. As illustrations I may refer to a few recent cases under my care: A man with syphilis had partial optic atrophy, hemianopsia, hemiplegia and considerable stupor. The above mentioned treatment was given him, and after some months his symptoms entirely disappeared, except those in relation to the optic nerves. Another man with progressive hemiplegia, beginning optic neuritis, and stupor, the condition suggesting brain tumor, recovered rapidly under salicylate of mercury. Another man with mild stupor and frequent convulsive attacks limited to one upper limb, and hemianopsia, also recovered promptly. The treatment of syphilis of the nervous system, especially with cranial nerve involvement, frequently must be continued a long time. The syphilitic palsy of ocular nerves I believe to be from implication of the nerves as they pass through the pia, and ocular nerves like other nerves may regenerate, but considerable time is necessary for this regeneration. I have seen a syphilitic external rectus palsy almost entirely disappear after it had been quiescent about ten months.

Positive laboratory findings with no symptoms of syphilis of the nervous system should be regarded with suspicion, but as Dr. Swift has shown, they do not invariably foretell the development of nervous syphilis. If other fluids of the body, as that from the pleura, could be examined in the early stage of syphilis they also might give positive findings indicating a general syphilitic infection. There certainly are late cases of syphilis of the nervous system with negative laboratory findings.

Oppenheim has shown that there may be focal forms of multiple sclerosis, a disease usually with diffuse lesions. I should like to make the same distinctions for syphilis. Implicating the nervous system, it usually is diffuse in brain and spinal cord, but there may be focal forms of nervous syphilis, and the lesion. meningo-myelitis, or meningo-encephalitis, may be almost confined to limited regions, as the lumbo-sacral, or the thoracic, or the cervical, or the medulla oblongata, or limited portions of the brain. There is thus a focal form of syphilis of the central nervous system independent of vascular focal lesions. There may also be occlusion of a definite artery from syphilis with a definite symptom-complex, and I have described several symptom-complexes of this kind, such as the occlusion of the vascular supply of the oculomotor nuclei with apoplectiform attack and partial or complete ocular palsy; or occlusion of the anterior spinal and adjoining vertebral arteries with loss of function in the median portion of the medulla oblongata, and showing clinically as paralysis of all four limbs with loss of sensations of position, passive movement and vibration; or occlusion of the anterior spinal artery in the cervical region with rapidly-developing paralysis of all four limbs, and sometimes with partial recovery, especially in the lower limbs.

Dr. George Walker (Baltimore): There have been two or three points omitted in this discussion for which I have listened very carefully. I hoped that they would be brought out. One is, how much syphilis have we in the community? None of the speakers have mentioned that point. I suppose they don't mention it because they don't know how much we have to deal with. It seems to me that it is an important point to discover. I should think that all the men who are concerned in its treatment would try first to discover how many people are infected. In the recent examination which I have

conducted in Baltimore in 1080 patients in the Johns Hopkins dispensary, without reference to what disease they came for (genito urinary cases excluded), there were 10.8 per cent. who gave a positive Wassermann. In the examination of 327 prostitutes, 67 per cent. were found to have a positive Wassermann, and a number were doubtful. The doubtful ones were classed with the negative. Thus we know that 67 per cent. of the prostitutes in Baltimore have syphilis. In 480 patients in the institute for the feeble minded in Maryland, I expected to find a high percentage, but it was low, less than 3 per cent. In 60 imbeciles there was only one with a positive Wassermann. In the jail, 600 inmates were examined and 24 per cent. were found to be syphilitic. In Spring Grove Asylum there were 11 per cent. In a boys' school which was taken as a representative school in Maryland, of 143, there was not a single positive test. In a lower grade of boys' school there were two of 56. In a shoe factory, in the examination of 63 men there were two positive. Another point is of tremendous importance, that is the inadequacy of treatment by hospitals. We talk about private practitioners, but here we find in some of the largest institutions treatment which is primeval is given. A man comes in with a gumma. He gets a dose of K. I. and we tell him to come back and that is the last we see of him. It is the same all over the country. We don't look after these patients. The lesion is healed and the man is lost sight of. It is time for the medical schools to stop this kind of treatment. We have instituted a special department for syphilis. It has not been working very long, but we hope it will accomplish a great deal of good. The cases are carefully handled and are followed up by the social worker. Every medical school should have such a department. I don't believe we need many beds for syphilitics. When we have a properly organized social service department they can follow up the treatment for us. We can render these people safe from danger of communicating the disease. Even with syphilitic sore on the lip, the most contagious lesion, with the administration of salvarsan the spirochetes will disappear. The social worker can do a great deal for these patients and we shall not have to keep them in the hospital.

Dr. Haven Emerson (New York): I cannot miss this opportunity to counteract the impression which I think must have been given by Dr. Cabot, that untrained legislators are responsible for

the requirements in various states and cities for the notification of venereal disease. As I remember it, the British Medical Association appointed a Committee which brought in a unanimous report, the first point of which was to the effect that the requirement for the notification of venereal disease was the first necessity for any campaign against syphilis and gonorrhoea.

It is true that the reporting of the disease, as required by health departments in this country, has not been honestly done or honestly required. It is true that the medical profession has opposed the principle and the practice of notification of venereal disease. The New York Academy of Medicine and the New York County Medical Society, at regular meetings, voiced their disapproval of the requirement for the notification of syphilis and gonorrhoea when this requirement was first issued by the Board of Health.

The dilemma which confronts the health officer is apparent. He cannot prevent or obtain treatment for these diseases unless he knows who is suffering from them. The organized medical profession has set itself vigorously against the reporting of these diseases. The medical profession in public dispensaries is giving a very inadequate and usually ineffective treatment for both diseases.

There are but half a dozen dispensaries in the whole City of New York to which patients can be referred by the Department of Health where the diagnosis and treatment will be scientific, thorough and complete.

If the reporting of venereal disease has accomplished nothing except the notification of cases in public institutions, it has called attention to the fact that the Department of Health is aware of the danger, is prepared to offer advice as to where treatment can be given, and put ignorant and helpless victims in the way of escaping the hands of the quack and reaching the sources of good advice.

Between 300 and 350 Wassermann tests are made daily in the laboratories of the Department of Health, and every one of these tests constitutes a notification of a case of disease, and this is no insignificant number of cases to be reported. Private physicians who do not report are hardly playing the part of public-spirited citizens willing to live up to the highest standards of their profession. If the community decides that we should not treat venereal disease through dispensaries operated at the expense of the taxpayers, the community should see that facilities are offered for treatment through existing endowed institutions, public or private.

We are at present in New York holding cases of active syphilis which are found among the inmates of correctional institutions. We prevent these prisoners from returning to their previous haunts until they are cured, just as we prevent patients with tuberculosis or smallpox from becoming a menace to the rest of the community.

The responsibility for the care and treatment of venereal disease rests upon the medical profession and the boards of managers of general hospitals. These two groups of people should combine to make available, at the earliest possible moment, such services as will tempt patients suffering from these communicable diseases to come for treatment and stay under medical supervision until cured.

The antagonism of the medical profession to the proper reporting of syphilis is essentially the same as its previous antagonism to the compulsory notification of typhoid fever and tuberculosis. Dr. Cabot is correct in stating that the notification as it is now performed by initial instead of by name and address, is neither logical nor complete and does not at present give us an exact idea as to the incidence of venereal disease in the community.

We found in testing the Wassermann reaction in a thousand push-cart peddlers that 8 per cent. gave a positive reaction. In testing 20,357 food handlers, examined by department physicians, 111 cases of positive reactions plus superficial lesions were found, which justified the refusal of a license to handle food.

It was the opinion of Dr. Biggs some years ago that dispensaries for the treatment of venereal disease should be established and maintained by the Department of Health for the sake of the public. Unless adequate facilities are shortly developed for the dispensary and hospital care of these diseases, the Department of Health of the City of New York will be forced, in the interest of the community, to undertake this method of preventing the spread of these diseases.

Dr. John A. Fordyce (New York): In reply to the statements of Dr. Patrick and Dr. Spiller, that equally good results could be obtained in the treatment of cerebro-spinal syphilis by the intravenous use of salvarsan combined with mercury, he said that if they would treat thirty or more cases in this manner and compare their blood and spinal fluid findings with those of Dr. Swift's and obtain as good results he would be glad to accept their statement. The

modern treatment of syphilis of the nervous system should be directed and controlled by accurate serological examinations and not by impressions or temporary alleviation of symptoms. He had treated many cases successfully by intraspinal injections after failure to influence their symptoms or their serology by the methods quoted by the previous speakers. A certain percentage of cases are arrested or relieved by intravenous and intramuscular treatment and this method should with certain exceptions be first employed. Where it fails or where a more rapid and immediate result is desired the intraspinous method is the one of choice. In tabes, cerebro-spinal syphilis and optic atrophy with positive findings in the fluid he had records of a large number of cases where the process had been arrested by intraspinal injections and the fluid rendered negative. The fact that our asylums contain numerous patients with incurable cerebral or cerebro-spinal syphilis treated in the manner outlined by the opponents of the intraspinal method furnishes the most striking demonstration of the need of a more scientific and efficient treatment than the one generally employed.

Dr. Homer F. Swift (New York): I wish to emphasize the fact that intraspinal treatment is auxiliary in nature. When general treatment, which should be tried first, is not sufficient, the intraspinal should be used. The table which is presented is given in the present form in order that our results may be compared with a similar series of patients in whom general treatment alone has been given. In comparing two such series it is important that the initial strength of the Wassermann reaction in the fluid should be known. As is evident from the table, in the patients with weaker Wassermann reactions treatment soon reverses the reaction to negative, while if the strength of the initial reaction is ++++ with 0.2 cc. or 0.4 cc. much more treatment is required, and in paretics it is often impossible to render the reaction negative. Therefore, for comparison it is more essential that a small group be carefully studied than that a large group should be reported in whom only a comparatively small amount of treatment has been given.

Dr. Hugh Cabot (Boston): I do not find myself in complete agreement with Dr. Dyer for I seriously doubt whether legislation would be a valuable aid in the enforcement of hospitalization. I

understood him to suggest the propriety of constructing special hospitals for syphilis. This I believe would be a most monumental blunder, since it would be of no benefit either to the patient or to the community. Nobody in their senses would go to a hospital constructed for the treatment of syphilis and the insane are already provided for. That pre-matrimonial certificates might be made out under the authority of the Board of Health is conceivable, but I fear that, as in every other attempt at compulsion, we should simply stimulate people to deception and I have no reason to believe that it would be effective.

In regard to what Dr. Emerson has just said, I do not think that he and I are fundamentally in disagreement except that he takes the resolutions of the last International Congress held in London more seriously than I do. A careful scrutiny of conditions under which these resolutions were passed has led me to the conclusion that they represented the views of a very small number of the delegates. If Dr. Emerson expects coöperation from the medical profession in treatment of venereal disease, I fear he will be disappointed. These conditions have been an immense source of revenue to the inexpert and the unscrupulous, and any measure which makes the treatment effective and tends to bring it into the hands of experts and under the control of the state will have to be carried out over the dead bodies of the medical profession.

THE PRESIDENT'S ADDRESS.

WILLIAM SYDNEY THAYER, M.D., HON. F.R.C.P.I.

Baltimore, Maryland.

TEACHING AND PRACTICE.

It would be impossible to address this Congress without a word of affectionate tribute to the memory of three great men who have presided over these meetings in years that have passed, figures, alas, that we shall not see again.

Fitz, the patient, discriminating student, the wise, inspiring teacher, whose keen eye and orderly mind shed light upon obscure corners of the art of medicine; Mitchell the poet, the brilliant physiologist, the acute and sympathetic reader of men's minds, the great practitioner; Trudeau the optimist who, in his long journey through the "valley of the shadow of death," led so great an army of sufferers to the land of light. 'Tis a heavy loss. But what a varied and lasting inspiration the lives of these men have left for us and for the world!

In the last several years, especially through the activities of the American Medical Association, the Carnegie Institution and the General Education Board, questions relating to medical education have been discussed very actively in America, and the changes and improvements in our methods of teaching and in the character and training of those who teach have been greater probably than in any like period in the history of American medicine.

The relations between teaching and practice in hospital and in university have of late been the subject of especially vigorous controversy in this as in other countries. To one who for five and twenty years has been engaged with more or less activity in the practice as well as in the teaching of medicine, who has been associated with two universities in which interesting experiments in medical education are now in progress, these discussions have been of absorbing interest.

With all the divergences of opinion and amid all the heat of discussion the goal aimed at is almost universally the same. It is our desire that the hospital, the school of medicine and the teaching staff shall be so organized that the ultimate service to humanity may be the largest; that we may gain greater knowledge of disease; that we may acquire more effective means, public and private, of recognition, prevention and alleviation of the many ills to which the human race and its inarticulate companions and servants are heir; that we may become more efficient in the care of our patients; that we may train better physicians. These are the main ends of the study of medicine. It has seemed to me well to devote this hour to a discussion of some of the phases of the relations between practice and teaching.

In the early days, the study of medicine in this country was begun in the office of the practising physician. By and by there developed schools of medicine in which the teachers were successful practitioners. The first of these schools were associated with hospitals, and although the body of teachers was not large, yet John Morgan, in his famous address on medical schools, early pointed out the necessity that special branches of medicine should be taught by men who had given their greater attention to these branches in practice. The professors of medicine and of surgery who bore the brunt of the teaching and directed their departments were usually busy men much sought for by the public in their community; and the teaching in the old days consisted largely of didactic lectures, with but limited demonstrations. Only thirty years ago, at the time when I was a student of medicine, the duties of the Professor of Theory and Practice consisted solely in the delivery of several didactic lectures a week; those of the Professor of Clinical Medicine consisted in the giving of two demonstrative clinics and one clinical conference. An assistant professor held one recitation a week. An occasional ward visit was given in one or another of the large hospitals, but these opportunities were improved by but a small proportion of the students. Physical diagnosis was taught during the second year to a class of about ninety by three instructors in several hourly exercises a week in sections of 20-30. This constituted the work of the department of medicine.

The direction of such a department was properly confided to a distinguished practitioner, a man of wide experience; and its management involved demands upon his time no greater than were

compatible with the suitable performance of his hospital and private duties.

In such a school of medicine the clinical instruction of a single medical department or unit could be, and often was carried out in a variety of hospitals—those hospitals with which the professors of medicine had the good fortune to be connected. The only association between the university and the hospitals was, in many instances, an amicable agreement on the part of the latter to allow instruction in the out-patient departments, through public clinics in amphitheatre and operating room, and to a certain limited extent in the wards. There were no university laboratories connected with the hospital. University laboratories existed at another centre which might or might not be near, or at a considerable distance from the hospital. These laboratories depended in large part upon the hospital for their material, but did not often, excepting through the good of the clinician and pathologist, control the supply; and, excepting to a very limited extent, the laboratories at the school rendered no especial service to the hospital.

In such a school of medicine a hospital was an accessory, a very close and valuable accessory to be sure, but yet an accessory to the department of medicine. And in discussing matters of medical education the hospital and the medical department of the university might be considered separately.

To-day the hospital must be considered not as an accessory to the department of medicine, but as its vital centre. One can scarcely conceive of a school of medicine wholly independent of its hospital. The laboratories for the study of the chemical and anatomical and physiological phenomena of disease cannot well exist at a centre removed from the hospital, or under the control of individuals other than those directly associated with the hospital management. On the other hand, the hospital in many instances has come to depend largely on the coöperation of the university in the performing of some of its most essential functions. Professors, assistants, undergraduate students all go to form a corps of hospital servants invaluable to the institution. In a word, the relations between hospital and school of medicine are so close and intimate to-day that a discussion of the organization of a medical or surgical clinic, or of a department of pathological anatomy, presupposes the assumption that hospital and university be under one management or in such close affiliation as to form a single work-

ing body. For the ends aimed at by both hospital and school of medicine are closely related. The main, specific purpose of the hospital is the care of the sick; that of the school is the training of physicians. The care of the sick can be carried out best through the employment of physicians of the highest order, and for these the hospital turns to the school. But to offer the student the best possible training the school must have opportunities for the study of disease and of pathological material, and for these opportunities it turns to the hospital. The delicacy and complication of modern methods of chemical and physical diagnosis demand laboratories and laboratory equipment which involve considerable and steadily increasing financial outlay; they call, moreover, for students of the best chemical and physical training to preside over these laboratories. This has brought it about that general hospitals which are not integral parts of a university must turn to universities for assistance, or spend, for the installation of independent laboratories and apparatus and for the employment of salaried heads of these departments, a sum of money which to many institutions is almost overwhelming. The university laboratories of bacteriology, serology, physiological chemistry and so forth where studies which are, in many instances, most practical, are to be made, should be in or adjoining a hospital. Thus the economy and mutual advantages of coöperation are clearly apparent. And more than this, in the true university hospital which is centrally situated, a community of interest is constantly drawing together the clinical and so called scientific departments. This is particularly true of the departments of physiology, physiological chemistry and pharmacology, and to the great mutual advantage of hospital and of university.

To-day in the better equipped and organized institutions there is in ward and laboratory, in hospital and school a common effort to contribute to the advance of the science and art of medicine in its broadest sense. Both hospital and school are centres of original research. However cordial and however free a coöperation there may be between the university and hospitals situated at a distance from the central plant, one must acknowledge the necessity to a modern medical school of one central hospital. And so it has come about that any discussion of the organization of a modern medical clinic presupposes that which, for purposes of illustration, may be called a "university hospital" as its centre, and calls for a consideration of certain hospital arrangements as an integral

part of the problem. Such a hospital should be organized upon a basis entirely different from that which used to prevail and still exists in many institutions. The medical clinic or the surgical clinic, if it is to do its full duty to the public, to the hospital and to the school, should be a well-organized unit under the control of a single director and a corps of associates and assistants. And of this corps of associates and assistants, some at least, preferably a considerable number, should be salaried men, who are required to give a large part of their time to their hospital and university work. All of these men should be members of the teaching staff of the university. Only in a clinic organized on some such permanent plan can constructive reasearch be carried out or systematic instruction given. The old-fashioned rotating service is incompatible with the ideals of a modern hospital or university.

According to the size of the institution one or more such clinics may exist, and there is no reason why, in a large hospital, there might not be two or more separate clinics, or why in a given university there might not be several more or less independent professorships of medicine with clinics at different hospitals, if the means were forthcoming to supply the necessary material for the full organization of such clinics.

But to return again to the organization and constitution of a single department of medicine as compared with that of thirty years ago. The changes in the method of teaching clinical medicine have been great. Demonstrative clinical lectures remain an important element of medical teaching. But the place of the didactic lecture has largely been taken by practical instruction before small groups at the bedside. This involves a considerable increase in the teaching staff and increases greatly the amount of time which the teacher must give to his work. Thirty years ago the professor of medicine may have been expected to give two or three hours a week to his classes. To-day he could hardly be expected to devote less than six or eight hours to personal teaching. The problems of the teaching of physical diagnosis in its restricted sense are not so different from those of thirty years ago; but to-day it is generally recognized that the university should offer the student far more individual practical training than he used to receive. In the old days, three men, let us say, were entrusted with the teaching of a class of ninety; to-day the work would be distributed among six or eight at least.

Thirty years ago there was no such thing as a clinical laboratory,

and clinical microscopy and chemistry were not taught in the medical department. Indeed, there were no special medical laboratories. To-day a modern medical clinic must, in the first place, control a clinical laboratory presided over by men who are called upon to give a considerable portion of their time to the training of the student in a large variety of methods of examination of secreta, excreta and body fluids; and this laboratory should also be a centre for scientific research. It was easy thirty years ago for one man to preside over an entire department of medicine and to conduct his practice as well. To-day it is extremely difficult, if not impossible, for a practitioner to direct the clinical laboratory and at the same time to do justice to his responsibilities as a physician.

Chemistry as related to the practice of medicine played a relatively small part in the medical curriculum of thirty years ago. In those days it was applied mainly to the study of urine, and these studies were for the most part of a simple character. To-day the chemical problems involved in the studies of human metabolism and used in the art of diagnosis are numerous and complicated, and are steadily increasing. No well-equipped medical clinic can exist without a department of chemistry, which should be presided over by a man of training and experience, capable of conducting and directing research and of overlooking the necessary studies of a variety of problems which arise in the wards of the hospital, for, as has been pointed out, no school of medicine can fulfil its mission to-day without intimate association with an adequate hospital. It is not easily conceivable that the director of the chemical laboratory could find time for medical activities outside the clinic.

The older methods of physical examination, so called, although mastered only by practice and experience, were yet mechanically simple. To-day, however, for the exploration of the human body and its activities, there are employed physical procedures which involve the use of instruments of great delicacy and demand an highly specialized technique. And sub-departments of radiology and electro-cardiography, each with its laboratory and its director, are necessary constituents of the modern department of medicine.

The medical clinic should also have a special department of bacteriology and serology, another sub-department the direction of which demands much of the time of an experienced student. Of these laboratories also the director should be one who is able to organize, conduct and stimulate research.

Again, there should be in association with every medical clinic a department of physical therapy for the study and application of mechanical, hydro- and electro-therapeutical methods; and especially for the teaching of massage and of general physical training. Such a department might, it is true, be under the combined control of affiliated medical and surgical clinics, but some of the responsibility for its organization and direction should lie with the chief of the medical service.

It has been said that the directors of these sub-departments could hardly be expected to give any essential part of their time to the practice of medicine. Are they therefore wholly to be removed from the care of the sick? Is the department of medicine to have under its control a number of sub-departments presided over by so-called "pure" bacteriologists, physiologists, physicists, chemists—men who are entirely removed from direct responsibility for the care of the sick? Far from it.

In the ideally arranged department of medicine, all of these men should have clinical duties and responsibilities—duties and responsibilities which, in a hospital, may be systematized. And in the properly organized department of medicine, although many of its members may in a sense be specialists, yet none will fail to acquire a wide general medical experience.

Let us now, for a minute, reconsider the problems which confront the director of a department of medicine to-day. The teacher of thirty years ago followed a relatively simple routine. The chief of a modern medical clinic finds himself at the head of a complicated machine, involving the appointment of a large number of salaried assistants, the manipulation of a considerable budget,—which alas! under present circumstances, rarely meets the demands of the situation—the co-ordination of a large staff of trained workers in clinical, chemical, physical, bacteriological, serological and physiological departments, and the organization of a system of group teaching to which he must himself devote a very considerable amount of his time. It is evident that the director of such a department should be a man who has had a rather broad training, who shall have had a basis of chemical instruction such as was impossible thirty years ago, and shall have spent a sufficient amount of time in work in each of the branches represented by the sub-departments of his clinic to enable him at least to comprehend the significance of the work which is there being done, and to carry out real supervision.

Time was when the teaching of medicine was, in great extent, a matter of authority. The student was led to accept precepts enounced *ex cathedra*. To-day the teaching of medicine is a matter of demonstration, of example, of practice. The student is inclined rather to distrust precept for which proof is not adduced; he is offered opportunities to study the symptoms of disease and its treatment by the bedside, and is instructed in methods by which he may control and confirm, so far as may be, the assertions which he may read in the book or hear from the lips of the instructor. The method of authority has given way to the method of observation and inquiry.

Who should preside over such a clinic as this? Who is the ideal director of the modern medical department? Thirty years ago the professor of medicine was properly he who had obtained the greatest reputation as practitioner or consultant. This reputation was often not attained before the age of fifty, and was gained through the active practice of the art. Such a man, who with years might or might not have attained financial ease, might suitably, in these days, have been called upon at a nominal salary, to direct a department and to give the two or three hours a week which were the sum total of the time exacted by the teaching duties of the professor.

But to-day it would be extremely difficult, nay, it would be almost impossible for a man with a considerable consulting practice to organize and direct a medical clinic, such as that which I have outlined, and, in addition, to do the amount of personal teaching which would be necessary. The practitioner, even if he be purely a consultant, is not master of his own time. He may limit his consultations to special hours, but he cannot cut off the increasing calls which appeal to his sympathy and come at any moment. And even if he see ever so few patients, he cannot control the complicating side-questions to which relations with any one ill human being are too apt to give rise.

With the consultant as with the practitioner *sensu stricto* the human influence is the most important element in his work. The preliminary conferences indispensable for the establishment of the necessary relations of sympathy between physician and patient, the interminable confidences of the nervous invalid, the unravelling of the tangled mental complexes of the psycho-neurotic sufferer, the heart to heart talks, the breaking of sad news, the straightening out of the many complications which so commonly arise in connection

with grave illness, the letters to physician and family, the interviews with friends and relatives—these, as the consultant well knows, are the duties that consume his time, but they are necessary and essential parts of his work. It is not the actual time that the physician spends in the study of his patient—that is often the smaller part of it. It is the accessory duties that render it impossible for such a man properly to combine active consulting practice with the responsibilities of the directorship of a large modern clinic.

To accept such a position would necessitate the abandonment of a large part of that physician's practice; this would mean the loss of the main source of his income, unless he were a man of independent means. If then the professor of medicine in a modern university is to be chosen from the ranks of those men who have acquired great experience through professional success, it will be necessary either that the university shall pay a very considerable salary, or that the professor shall be a man of independent means. Such a salary, unfortunately, if men of this class are to be obtained, would have to be quite beyond anything that is at present possible in most universities. The successful consultant is usually put to considerable expense for the maintenance of the machinery necessary for his work, and in many instances comes to maintain a sort of existence which involves large financial responsibilities. However much such a man might desire to avail himself of the fascinating opportunities offered by the directorship of a large medical clinic, it is too commonly the case that by the time he has well entered upon his fifth decade he has already assumed responsibilities toward others which make it impossible for him rightly to abandon the sources of his income. But this, it seems to me, is not the essential feature of the situation. Is the physician who through years of practice has become the successful consultant, the man who is best fitted to direct a large department of medicine or surgery? By no means always. Indeed, in the majority of instances, it is another course of life which should best fit a man for a university professorship.

There has arisen gradually in this country a new class of consulting physician, the man who has deliberately planned his career from the outset, who has sought through long years of study in hospital and in laboratory, in association with large clinics, to gain in a concentrated fashion, as it were, that experience which may make his clinical opinion, both from a diagnostic and therapeutic stand-

point, most valuable. Long-continued service in institutions in which proper opportunities for study and research are offered, is giving to the public to-day a number of men who, while thoroughly trained and practised in modern methods of diagnosis and treatment, have accumulated at a relatively early age, a store of actual clinical experience such as is acquired in independent practice only after a much greater time and, in the majority of cases, with a loss of touch with some of the more recent advances in medical science. These men, the products of intelligent methods of hospital management and organization, are as a rule soon called on by their colleagues in more active practice, for advice and assistance as general consultants. Men who have pursued such a career, which has inevitably involved at the outset a considerable financial sacrifice, are usually men of scholarly tastes who keep in touch with laboratories in which they may continue research and coöperate with their colleagues in practice in the study of the nature and treatment of disease. It is from this class of men that the professorships of medicine are more and more likely to be filled. Such a man may well enter upon a professorship by the time, or even before, he is forty years of age.

This leads us directly to one of the questions which has been most actively discussed of recent years: Is a man who has obtained his clinical experience largely or purely in hospitals, properly fitted to teach students the essentials of the practice of medicine?

A distinguished student of the problems of medical education has been quoted as saying essentially: "Diseases are the same in the rich and in the poor, in human beings and in animals. To the clinician the ward is his laboratory, and the study of disease in the patient in the ward is, in all essentials, the same as the study of disease in the animal in a laboratory. The only difference between the study of disease in hospital and outside is that in the hospital the patient may better be observed. It is a mistake to say that it is necessary for a professor of medicine to have had experience in private practice when the same experience may be obtained more intelligently and in a much more concentrated form in the hospital."

This conception, which has, by some, been regarded as characteristic of the point of view of those who have favored the establishment of professorships of medicine on the so-called "full time"

basis, has been looked upon as fallacious and dangerous by many of the opponents of certain modern tendencies in medical education.

"No man," they say, "is fit to teach students the art of the practice of medicine who has not himself passed through the experiences of the practitioner. Practice in a hospital ward is one thing; practice in the home of the patient, another. He who has been accustomed to rely on the trained nurse and on the many appliances and instruments of precision which a well-appointed hospital affords, can have little conception of the difficulties which he will encounter in private practice. He whose only experience has been with the trusting, unresisting patient in the general wards, will find himself at sea when treating the whimsical, critical, prejudiced, opinionated invalid in private life. He who has been accustomed largely to study serious diseases in the wards of the hospital will have small sympathy with, and little understanding of, the trivial complaints of the supersensitive and nervous members of the more well-to-do classes. The conditions that he is called upon to treat are to be remedied in great part by minor regulations of habits and manner of life, of eating and drinking and smoking and exercise. His main duties consist in ministering to the minds of his patients—in kindly counsel and encouragement—in advice tending toward the alleviation of a thousand petty ills which he who knows that they will pass with time, does not even consider in himself—which the less sensitive patient in the ward barely notices. How can one who has never had this experience teach students the art of practice? Is it not folly to take away the teaching of medicine from the experienced practitioner and to give it to one who has had a training which might almost be called academic? Must we not regard this idea as the dream of the layman and of the laboratory student who, with all his scientific attainments, is yet woefully ignorant of the conditions of the doctor's life and of his duties."

There is much truth in these objections. I should have no hesitation in agreeing that the medical experience suitable to qualify a physician as a consultant or a teacher of medicine cannot well be obtained wholly in the free wards of a hospital. There is a great difference between the mental workings of the patient in the free ward and those of the average individual with whom one is thrown in private practice. The stolid indifference to outside influence shown by many patients in the general wards renders the study of

disease in hospital not so very different, it is true, from the study of disease in the laboratory, but so soon as one becomes associated with patients of a higher mental order, problems in diagnosis and in treatment arise which are much more difficult and complicated. It is, it seems to me, not easily possible for one who wishes to fit himself for practice as a consultant or for the teaching of medicine to gain that experience which he should have without a considerable association with individuals of more complicated mental constitution. Moreover, there are certain diseases which, strangely enough, are rarely seen in the free wards, yet are common in outside practice, diseases the recognition and management of which are of the utmost importance. I need refer only to angina pectoris. A man who is not familiar with the mental attitude of the people among whom he or his students are going to be thrown, who has not learned by experience successfully to navigate his bark through the mist of accessory problems which befog the antechambers of the sick room, is unable to give to the student much that will be of real value in the practice of medicine. But fortunately in many hospitals to-day, the great development of private wards offers abundant opportunity for the acquisition of just this experience. The man who desires to fit himself for a position as teacher of medicine or consultant should spend a considerable period of time in practice among the class of patients which is to be found in the large private departments of many of our hospitals. Such an experience gained in the hospital, will afford him in concentrated manner just what he might obtain otherwise through a much longer period of time in private practice.

This is the general course of training which the aspirant to the professorship of medicine is likely in the future to follow. His elevation to the directorship of a large department of medicine or surgery may be directly from the clinic in which he has occupied a salaried position and to which he has given his entire energies, or it may come after some years of consulting practice during which he has preserved close relations with an active clinical department.

Recognizing the magnitude of the problems associated with the organization of a large medical clinic, it has been felt that such a department could best be presided over by men who were able to give their whole energies to the university in organization, in teaching, in the conduct and direction of research. And, notably at that institution with which I have been connected for more than twenty-

five years, several of the clinical departments have been re-organized upon a university plan. Through the generosity of the General Education Board, the institution has been enabled to establish a staff of university professors and salaried assistants who take charge of these clinics for hospital and university. These men, freed from the calls of outside practice, are able to give their entire time to the service of the department in the care of patients, the promotion and conduct of research and in the teaching of medicine. And as is well known, the members of this staff have agreed to abstain from the practice of their profession for their own emolument.

The discussion associated with this experiment has been very active, centering largely upon the last-mentioned circumstance—the withdrawal or abstention of the university professors and their assistants from private practice. Those who have objected to this procedure have regarded the plan as unwise and even unfair to the physician himself, to the hospital, to the students and the the public.

In the first place, with regard to the professor himself, it has been pointed out, and with justice, that there can be little relation between the salary which the university could or should pay to the professor of surgery or medicine and the gross income of the successful surgeon or consultant in a large city. It has been asserted that the opportunities brought by a considerable income for wide associations with the world at large are broadening to the character of the man and are indirectly of value to the institution with which he is connected; that furthermore it must be a very serious question to the physician himself whether he is justified in planning deliberately a manner of life which can never lead to wealth or real financial freedom, when there might be open to him an opportunity to give to his family and those dependent on him the advantages which come with a large income. Is he not, it is asked, giving up the "larger life" for the smaller, and will not the university in the end suffer by the loss of the wide domestic and international relations so often established by the professor who has the material resources to visit his distant colleagues in their clinics and to entertain them at his home? Will not the hospital, more directly, lose in the absence of those cordial relations which arise to-day from the association, as a consultant, between the chief of the medical clinic and the practising physician?

Will not the students suffer, it is asked, through their association only with men who have had a more or less academic training in a

hospital, who are out of touch with the exigencies of actual medical practice? Will not practitioner and consultant suffer seriously in losing their control of the hospital material which is now to pass wholly into the hands of salaried men? And will not the public suffer? May it not indeed be regarded as an injustice to the public and to the practitioner that they should be denied the services of these men especially eminent in medicine or surgery, whose opinions presumably are of special value—these men who have been chosen to direct large clinics?

It cannot be denied that these objections have a certain force.

The physician who, starting from modest beginnings, has, by hard work, acquired a large income cannot underestimate the blessings and the opportunities that such a revenue brings to him and to those who depend upon him. But such incomes are rarely honestly gained without very hard, very confining work, and without real intellectual hardship to the practitioner if he be a man of scientific tastes or aspirations. To one who has the temperament and ideals of the student, the advantages of a university professorship cannot but appeal very strongly. No man who covets a fortune should select the career of a university professor. He who enters upon such a life knows from the outset what his income is to be, and what the outlook for his family. He cannot expect to be a rich man, and he must plan his life accordingly. But the compensations are great to one of scholarly tastes. The opportunities for study and research offered by the university clinics and laboratories, limited though they may be at certain times by the demands of teaching, the freedom from the uncertainties, the complications, the endless activities of the life of a busy practitioner or consultant, the hours for reflection, for rest, for recreation offered by the stated vacations—these, wholly apart from the privileges and responsibilities of the organization of a large department, are advantages so great that they will always attract men of the highest order.

"And the larger life?" Who can say what "the larger life" is in itself? The "larger life," alas, does not always go with wealth and that which surrounds it; and who shall say that the opportunities which come to the university professor of distinction and to those about him, are more restricted than those which are open to the practitioner and consultant? Certain of the luxuries of life the professor may be obliged to eschew, but there are other privileges which will be his that no money can buy.

It is true that the salary of the university professor has not, in general, advanced with the incomes of those about him, or with the general scale of living; and it is, I believe, folly to attempt to put the directorship of clinical departments on a university basis at salaries such as have been in the past offered to the professors in the strictly scientific departments. Nevertheless, no one can expect such salaries to be large as compared with the income of successful men in private practice. It should, moreover, be remembered that with the successful consultant, for instance, nearly one-half of his gross income is often absorbed by the legitimate expenses of his practice. The burden of these expenses is lifted from the shoulders of the university professor whose fixed income represents a revenue of nearly twice that size with the consultant.

But the salaries of university professors, whether in clinical or scientific branches, should be materially—very materially larger than they have been in the past, if these men are not expected by outside activities to add to their incomes. I can, however, see no reason why the salary of a professor of medicine or surgery should be larger than that of a professor in a so-called scientific branch. In business circles it is true that the salary depends purely upon the immediate market value, so to speak, of the individual; that he who can in the world of affairs earn but a modest sum is able to demand a far smaller salary than a man with large practical earning capacity. The physiologist who devotes himself single-heartedly to his teaching and his researches might, if thrown on the world to earn his living, have but a relatively small earning capacity; the clinician, if he have attained a popular reputation, may, on the other hand, be in a position to make a considerable revenue.

Universities often obtain the undivided services, let us say of the professor of physiology, for an amount which was once but is not to-day a proper living salary for a man whose abilities and contributions to science entitle him to a comfortable and prominent position in the community; that position which it is to the advantage of the university that he should occupy. And such professors in many institutions sacrifice much to the cause of science.

This seems to me fundamentally wrong. These distinctions must eventually be removed, unless our universities are to remain as short-sighted as our National Government and bring it about that our professorships, like our diplomatic posts, shall come to be situations which only men of independent means can fill.

But to return to the question of the professorships in the clinical branches. If the salary be adequate, there should always be efficient men whose ambition will be to occupy chairs of medicine and surgery even though they realize fully that the chances of the acquisition of a large income are small.

The objection that is so commonly raised as to the injustice and unwisdom of any understanding or agreement by which the directors of the departments of medicine and surgery should abstain from private consulting practice, is one which, as a teacher and practitioner, has interested me greatly. As has been indicated before, it is not easy to see how the director of a modern university clinic, or the chief of a service in a large hospital organized on a similar basis, can give any essential part of his time to outside consultations. According to the tastes and character of the man, he will probably give more or less of his time to private consultations at his clinics. To the consultant the puzzling and interesting pathological problems brought for his consideration by patients sent to his consulting room by colleagues at home and abroad, form the most valuable part of his experience. Such patients the professor of medicine and his associates will doubtless continue to see. They should form a great addition to the hospital clinic. Some of these patients they will desire to admit to the hospital for study. But these consultations the director of a large clinic could hold only at stated periods, and to this work he could give only a limited amount of time. It is difficult to see how it would be possible for the director of such a clinic to give the proper service to his department, and yet conduct anything like an active consulting practice outside the institution. Under exceptional circumstances, however, the professor will probably accept calls to outside consultations, but only under exceptional circumstances. The director of a large medical department must control his own time and his engagements. He who is openly occupied in general or in consulting practice can never truly be master of his time.

A curiously active discussion has arisen upon a rather small point in connection with the practice of the salaried director of a medical clinic. In some clinics, as has been said, the understanding exists that the professor shall contribute whatever fees he may collect from private patients to the departmental funds. This procedure has excited vigorous criticism and opposition; it has indeed, been

considered fundamentally improper, subversive of the higher interests and principles of the medical profession.

This is a problem on which I have meditated seriously, and, look at it as I may, I cannot but regard it as a rather small and relatively unimportant detail of a larger general question. The professor should naturally demand suitable compensation for his services to private patients. But whether such compensation should go directly to him, or should be turned over by him to the budget of his department, seems to me a matter of detail to be settled between him and university or hospital. I am at a loss to understand the attitude of those who see in this a question of principle.

Some time before the first experiment of a university medical clinic was put into practice, a distinguished clinician whose services were sought by a well-known institution, offered independently, a plan for the organization of his department, which is very similar to that which now exists at the Johns Hopkins University. This offer outlined the establishment of his professorship upon a purely university basis, with the explicit understanding that the income from any private consultations into which he might see fit to enter, should be added to the budget of his department. Such an arrangement might be regarded as a distinct protection to the professor. For the financial questions which relate to practice are to some annoying and disturbing. And if the salary paid to the university professor be in any way sufficient, I can easily fancy that the professor might prefer to have it understood that the income from any practice which he might care to undertake should go into the budget of his department. I can also fancy that others might feel differently; that they might prefer a complete independence, expressed or implied, in this respect. I can further fancy that the university or hospital might fear that if the professor once began to accept fees from private patients, he would be in danger of being drawn into practice to such an extent that it would interfere with his university or hospital work. But, as I have said, the question of what becomes of the professor's fees seems to me of limited importance—a detail in connection with the larger problem. I cannot see in it a great question of principle.

So far as the student goes, the danger that under the direction of a salaried professor, he may be given a training more purely academic and insufficiently practical seems to me small. In the

first place, it has already been pointed out that the professor of medicine will doubtless be a man who has had a considerable clinical experience with patients in all classes of life, whose training has been by no means purely academic, and although some of his associates will perhaps be men who have not yet acquired the ripened experience which should be that of the head of the department, yet no one for a moment fancies that *all* the instruction in medicine and surgery will be given by the nucleus of teachers wholly dependent on their salaries. In every large clinic, and in every large hospital affiliated with a university, a considerable part of the instruction in general medicine and surgery, as well as in specialties, must be entrusted to men with or without salaries, who are more or less actively engaged in practice. The fancy that because the director of such a clinic and many of his assistants are no longer at the beck and call of the public, the student is to be regarded as deprived of the opportunities offered by association with men who have been or are engaged in active practice, is a misconception.

That which the re-organization of a clinic upon a university basis should do, however, is to bring it about that the practitioners who share in the work and advantages of the hospital and take part in the instruction, may be rather more carefully and wisely chosen than they have been in the past. Well-digested experience, merit and teaching ability should more clearly and surely be recognized by a director untrammelled by hospital traditions and bent solely on the improvement of his clinic.

The experienced clinician who is still engaged in private or consulting practice, if he be a man of high order, is not likely to lose his touch with the hospital or with the clinic so long as he is able and desirous of giving it his services. Indeed, it is probable that in the future, institutions will retain a closer connection with some of the members of the staff who are engaged in private consulting practice by offering them the privileges of consulting rooms at the hospital. This plan, which has already been adopted in some instances, ought to be of great mutual advantage to hospital, to physician and to patient. To the hospital because it brings into close connection with the clinic those instances of rare and unusual disease which are sent to the consultant; to the physician because he is able to give much more time to his work at the hospital; to the patient because if the consulting room of the physician be at the hospital center, the many accessory examinations which so often

have to be made, can be carried out much more expeditiously. But if such a physician be engaged in active consulting practice, he will no longer be the director of the clinic, and this, as has been pointed out, would seem to be desirable from every standpoint. For only under exceptional circumstances can such a man command the time necessary properly to direct a full department.

How much or how little time the head of a department of medicine or surgery may give to consulting practice is, however, a question which in the end must depend entirely on the character of the man. He may give very little of his time; he may give a good deal. But if he be a man whose living interest is in his clinic, it matters little. For in either instance, through the character of the men that he associates with him, he will see that his department does its best work.

The objection so often raised that there is danger that a professor of medicine or surgery who abstains from outside consulting practice may be removed from touch with the profession, is comprehensible but not, I think, serious. If the director of the department be one who does a considerable amount of clinical work, he will still keep in active touch with the medical profession even though his consultations be held only at the hospital. In any event, the work of the department itself, set forth by him and by his associates and assistants in public clinics, in medical societies, and in journals, should keep him well before the eyes of the medical world.

The tendencies of the hour would seem to indicate that a very large nucleus of the staff of the medical or surgical clinic will in the future consist of salaried men who are giving the greater part of their time to the activities of the department; and it is very interesting that not only in hospitals affiliated with university schools of medicine, but in other independent institutions, this idea has already taken root. The experiment of a generously salaried staff of physicians and surgeons who are expected to give the greater part of their time, if not their entire time to the institution, is already being made in various hospitals.

One of the most important functions of a modern medical or surgical clinic is that it should afford opportunities for the ambitious student with scientific aspirations to pursue that course of study and acquire that experience which will fit him for a university career. Every year there graduate from our schools of medicine men with the ideals, aspirations and abilities of the true student, who, because

of financial disability, are obliged to enter directly into active practice. A certain number of these men preserve their enthusiasm, make the most of their opportunities, and return later to the pursuit of those studies which have always been the object of their ambitions. Some find unexpected intellectual satisfaction in the varied opportunities offered by the life of a practitioner. Others, dazzled by the financial rewards of success, lose their early ideals. Many, however, are obliged to give up their ambitions. With the organization of the modern medical clinic, there should be a considerable number of assistantships commanding salaries which should make it possible for many of the really good men to pursue their chosen career. And it is highly desirable that such salaries should be sufficient and so graded that these men, if they prove themselves of suitable character and ability, may continue their work through long years.

But—and this is a question very often raised—what about the opportunities for the development of practitioners or consultants if every medical or surgical clinic become a training school for professors of medicine? The answer is simple. The training which best fits a man for a professorship differs in no way from that which best qualifies him for the career of a practitioner or consultant. Some of the men who start upon their career in a modern department of medicine will remain connected with the service in one capacity or another for ten or fifteen years or even more, until the offer of a position as assistant or professor or director in another large clinic comes to them. Many, after eight or ten years experience, will find themselves well fitted to enter into the practice of medicine or surgery as consultants. Others after spending a shorter period of time will doubtless take up general or special practice. That to which we may look forward with reasonable certainty, however, is that the re-organization of hospital and university clinics according to this general plan, the essential feature of which is the establishment of a large nucleus of salaried men who give the greater part of their time to the activities of their service, will provide for university, hospital and public a body of men better trained and with richer experience than has been offered in times past.

There is one point in connection with the re-organization of the clinic upon what I have called a university basis which seems to me of real importance. This has been touched upon especially by Dr.

Meltzer (Science, 1914, XL, 620-628). I refer to the desirability of ample provision for voluntary assistantships. This is a matter which touches especially hospital organization. The work of a modern hospital clinic has changed greatly. A well-organized medical or surgical clinic is as truly a scientific department as are the university departments of anatomy, physiology and chemistry, and in every hospital there is a constant demand for more and more students to assist in the researches which are being conducted by the various sub-departments, and incidentally in the care of the patients. The great advantage to a hospital of the presence of students in its wards has often been pointed out. Such students form a corps of extra assistants who enable us to study and care for our patients much more intelligently.

But where can one find the director of a medical clinic who is not longing for the services of more young men, recent graduates with scientific aspirations, to assist him in the study of a variety of different problems? As it is to-day, only those men who can obtain salaried positions upon the staff or are of independent means can afford to give the time required for such studies. But many a student, upon his graduation, and during the several years that follow, would be more than willing to accept a position as voluntary assistant if he might be given a room and his lodging in the hospital. Every modern medical or surgical clinic should have a number of these positions open to such men as the professor may see fit to select. There could be no better investment for the hospital. Research assistants should be considered as essential to the welfare of the hospital to-day as are the regular internes.

These are the considerations that I have wished to bring before you to-day. They have to do with matters which are not without public significance.

The relations of the medical sciences to the commonwealth are of great intimacy and of vital importance.

Time was when the physician was called upon only to minister to his ill or wounded fellow. To-day he is something more than the healer and the binder of wounds. The advice of the medical scientist is sought in every sphere of human activity. It is he who is called upon to outline and direct those measures which protect

our homes from epidemic, our cities from pestilence. It is he who has opened the wealth of the tropics to the safe exploitation of man; to him we must look for that counsel which shall preserve the efficiency of our armies in the field and of our cohorts of industry at home; which shall lessen the horrors of war and the dangers of peace.

No effort can be too great, no sacrifice too costly that may afford to the student of the medical sciences the most active stimuli, the best opportunities for training and for research. For in the training of the student of medicine is involved more closely than is generally realized, the prosperity and safety of our country.

THE UNDERLYING PROBLEMS OF IMMUNIZATION.

THEOBALD SMITH, M.D.,

Princeton, N. J.

The underlying problems of immunization are two-fold. We have in the first place the plain, practical problem to prevent or to check diseases by applying methods copied from nature and improving upon them in the interest of man, if possible. Secondly, we have before us the problem of discovering the modus operandi of resistance to disease, the sequence of events which are associated with recovery on the one hand and with complete resistance on the other.

The object of immunization is to raise the resistance of the body from a lower to a higher level. How much this elevation will be depends on the character of the disease; this, in turn, on both host and infectious agent. The remarkable effectiveness of smallpox vaccination has left the impression that immunization towards any disease always means complete protection from that disease. We miss here the quantitative concept which is involved in all life processes. Perhaps the spectacular success of Pasteur's Pouilly-le-Fort experiments with the vaccination of cattle and sheep against anthrax in 1881 gave an impetus to the belief that vaccination, to be such, must or will be completely protective. In Pasteur's early test we see the element of chance or luck which accompanies the birth of all great ideas. The disease he chose was admirably adapted to illustrate the process of immunization in its most favorable aspects. Almost any other disease might have left it undemonstrated. If Pasteur had been armed with recent methods he might have found attenuated anthrax bacilli from the vaccine used circulating in the blood of his vaccinated sheep for a time, as was shown by Sobernheim by his simultaneous method of using vaccine and serum many years later. If it were a general property of the anthrax bacillus to produce internal localizations beyond points of entry, such vaccinated sheep might have developed later various lesions.

We must, therefore, accept the fact that no kind of vaccination will be invariably and completely protective. We may hope to con-

vert a fatal into a non-fatal attack, a mild attack into one so mild as to remain unrecognized, or into complete protection. As long as the susceptibility of individuals varies towards the same infecting agent we cannot expect the same treatment to bring all to the same level of resistance. Nor is it possible with the same treatment to protect equally well against agents of high and low virulence. Granted that the exposure following immunization may lead to disease so mild as to remain unobserved, it follows that if at this particular juncture the individual subjects himself to very unusual, depressing conditions, the infection may develop into a typical attack.

It is therefore important that we do not lose sight of the quantitative side of immunization. To neglect it tends to bring the process into discredit because our claims cannot be justified. One of the problems bearing upon this phase of the subject is a better study of spontaneous, mild disease as a result of exposure in the vaccinated individual and of attacks which may not be recognized by clinical methods and which even the patients themselves may overlook. For our present conception of acquired immunity tacitly assumes that after every exposure there is some, however slight, multiplication of the virus necessary to wake up the immunizing mechanism.

The concept that immunization is quantitative is readily illustrated in laboratory experiments. A disease which is invariably fatal to the rabbit, even after the feeblest cutaneous dose, may be so modified by preliminary immunization that life is prolonged. The original septicemia assumes some other aspect. It would seem as if the infection were driven or kept out of the blood. It localizes in serous cavities and multiplication in the peritoneal, pleural, and pericardial surfaces follows. A higher immunization eliminates these and we have next localization in the skin, the subcutis, the joints, the central nervous system, and so on. In some cases the septicemia is replaced by a local process of undue proportions where the test virus is deposited. The animal seems well but the process slowly extends.

In most human diseases the situation to be met is not so serious. Nearly all established infectious diseases depend for their continuance on the recovery or the prolonged existence of the host. This unstable equilibrium is the result of natural causes. We are

therefore not dealing with diseases like those of the laboratory which usually end in death. The amount of resistance to be added to that already possessed should, by processes of artificial immunization, bring the level of resistance up to more or less complete resistance. In working out such problems of immunization the essential factor to be kept in mind is to raise such resistance with the least injury to the subject.

The direction which immunization is to take depends on the etiological factors involved. We know that there are primary and secondary infectious agents in most diseases. It is not improbable that the latter may become more numerous and more widely distributed under conditions as they are shaping themselves to-day subject to the influence of an increasing density of population. It is generally conceded that if we protect against the primary agent, the others are thereby kept suppressed. The assumption underlying this view is that the secondary agents play no part in giving the primary agent an opportunity to infect but that the reverse is true. It is probable that light may be shed on this subject by more intensive study of the effects of immunization towards animal diseases. It is claimed that immunization against the filterable virus of hog cholera disposes of the many secondary infections associated with it. But this claim requires a careful study of the vaccinated animals or of the residuum of unsuccessful vaccinations. This is usually not done for want of time or because its importance is underrated. In general, however, the weight of opinion rests on the side which assumes that the suppression of the primary or main factor takes care of all the rest and that they themselves are enabled to invade and multiply because the primary disease preceded them. When we come to the actual outbreak of such a possible chain of diseases the situation is changed. The main or primary disease, usually a highly adapted and specialized virus, is not, as a rule, fatal by itself and would run its course satisfactorily if so-called complications can be kept away. The question at issue then becomes a choice of vaccines towards possible secondary invaders. Such a question would probably not present itself until some plague arose whose malignancy was due mainly to some associated and highly virulent but easily cultivable micro-organism belonging to some such well-known group as that of the streptococci, staphylococci, paratyphoid bacilli, etc. The European war will eventually disclose to us prob-

lems of this kind. Notably the appearance of paratyphoid diseases after anti-typhoid vaccination will receive due attention from this point of view.

The persistence of vaccinal immunity and that due to the actual disease has been the subject of prolonged discussion. Notably the immunity against smallpox, owing to the legal aspects brought out by compulsory vaccination, has been statistically investigated with the result that its limit is not a lifetime but seven years, more or less. The general rule that a single attack of a disease protects for life is subject to limitations. All acquired immunity is a perishable commodity. The question is complicated by several factors. The human and animal body become more resistant to infection with age. The young animal is far more susceptible than the adult. This high susceptibility was utilized by Pasteur in raising the virulence of cultures. It was demonstrated by Metchnikoff with Asiatic cholera on nursing rabbits and by Bang with avian tubercle bacilli on colts. The difference is not simply a matter of body weight. To get light on this phase, statistics among adults over a certain age as to freedom from certain infectious diseases would be of value. To my knowledge no such statistics have been gathered, except in hospitals. There is also the other complicating factor of reinfection without clinical signs which would maintain and strengthen any immunity acquired in infancy and childhood. The prolonged persistence of acquired specific immunity as such and our subsequent protection as a result of early attack is to my mind unproved.

There is a clearly marked distinction between groups of micro-organisms as to the capacity of the host to be immunized experimentally. With some the attempt is much more readily successful than with others. Those bacteria which act only through their toxins are most easily kept in check by immunization. Next come the acute, septicemic diseases, such as those due to bacteria which are quite perishable, including the group of pneumococci and bi-polar bacteria. Bacteria producing diseases of longer duration appear difficult to suppress in proportion to the chronicity of the affection. To these general rules there are, of course, exceptions.

The problem of immunity due to geographical factors is one that will receive more attention since the pressure of the inhabitants of temperate climates towards the tropics is destined to grow rapidly. Geography, as such, has no recognizable influence for we

have been told by students of tropical diseases that immunity or susceptibility of any given group towards a disease depends, not on latitude or climate, but upon the prevalence or absence of such disease in the home of that group. Endemic disease leads to relatively heightened resistance. Since most of the diseases in question are due to parasites which survive the attack and may persist in the blood during lifetime, which, in other words, are able to subsist in an immune host, the most rational explanation is that based on the transmission of immune bodies to the offspring. This phenomenon binds the various generations together and the affected species may be said to be under the continuous influence of the parasites. If we add to this the elimination of highly susceptible individuals and the random selection of any individuals tending towards a greater histogenic resistance, the hope that we shall be in position to prepare artificially, by immunization, the white man to meet tropical diseases does not seem very near. Here natural selection and elimination will have to play a part unless we attack the problem from the other end and suppress the disease by destroying the intermediate hosts and other favouring external conditions.

Coming now to the conditions to be met in the body itself, the problems to be solved are the same as those which confront us in endeavoring to unravel the complexity of the processes of infection and resistance. Though it is safe to assume that the fundamental biologic principles governing parasitism and resistance to it are the same for all forms of life, yet the application of them is so diversified, the rearrangements and groupings of processes so manifold that the only solution is the investigation of a given disease by itself from every point of view and with help from every source. Just what types of disease should be so studied will depend, not on practical results or expedience, but upon the principles likely to be unearthed. They may be human or animal, but they must be natural and not induced diseases. When a few diverse diseases have been analyzed in this way we shall probably be in position to anticipate at least what the intimate processes of most other infectious diseases will be found to be. When we have reached this level, the choice of a vaccine or an immunizing agent may then be simply a question of technique rather than one of fumbling in the dark. But medicine cannot be expected to wait for such results. Empiricism in science frequently wins triumphs and science records and classifies the result, not because it is inefficient, but because the

opportunities have been lacking to develop our knowledge in orderly manner.

Among the well-established facts in immunology is the greater efficacy of living virus over any other. This has been tested by Pasteur on anthrax; by Strong on plague and Asiatic cholera; by a number of workers on bovine tuberculosis. It has also been frequently shown to be true in the laboratory on smaller animals. The changes induced by living virus approximate the natural disease most closely and this mode of immunization should be taken as the point of departure for all others. The practical application, however, encounters many obstacles. There is the degree and permanency of the attenuation or reduction in virulence which must be carefully considered. The preparation of the vaccine, therefore, even when a reliable method of attenuation is available, could not be left in the hands of irresponsible routine workers.

A serious drawback to the use of bacterial vaccines is the highly developed specificity of the immunizing properties. In early work on immunization it was hoped that related but harmless bacteria might do for vaccines, but it was soon found that they were useless. Why the colon bacillus should not produce active immunity towards its relatives, the paratyphoid bacilli, seemed strange. Gradually the circle of immunizing bacteria was drawn even smaller. It became the generally accepted view that the strain producing the disease yielded the best vaccine against that disease and the more recent work of Neufeld and of Cole and his co-workers demonstrated that even pneumococci must be carefully differentiated and that a given therapeutic serum protects only against the strain which called it forth. These facts go far to prove that the so-called immunological relationships are relationships which are evolved and perfected by parasites under the influence of the host to which they have become adapted. They represent highly specialized and refined modifications not determinable by morphological or cultural methods. They are the specific acquisitions of micro-organisms which have passed from the free to the parasitic habit. They are likewise the first to be lost when facultative parasites are permitted to multiply indefinitely on our culture media.

In spite of the various objections to the method of living vaccines it is the coming method, not perhaps in our day. The opportunities for improving and fixing the vaccinal value and safety of immunizing strains have not yet been exhausted and here, as in other

directions of preventive work, we must look to the results obtained from animal pathology in its dealings with natural diseases to give us courage to proceed.

Besides the attenuation of homologous viruses, the finding of naturally attenuated strains is a possibility to be considered. The preconception that strains of very low virulence cannot immunize toward highly virulent strains should not stand in the way of actual trials. Recently P. B. Hadley described an almost avirulent strain of fowl cholera virus which protects rabbits against death from a highly virulent strain fatal within 36 hours. The protected rabbit develops a large local lesion, however. The fact that, for example, pneumococci lose their virulence very promptly in cultures and that such avirulent strains do not immunize does not apply to other species of bacteria, the virulence of which is lost gradually.

Next to living virus, the bodies of bacteria killed by heat seem a priori to have the best chance for producing immunity. Here also the success or failure with one group of micro-organisms must not be permitted to anticipate results with other groups. This procedure is now used very widely, though with what result statistics alone will tell. The success or failure will depend theoretically on what in the life of the micro-organism is chiefly responsible for the production of immunity, in other words, what is the important antigen. If certain ferments or toxins secreted by the micro-organism, or certain metabolic products, are the means of offense or defense, dead bacteria may be of slight avail as the manufacture of such agents is stopped by death and the bodies of the bacteria could not contain more than traces of such substances. If, on the other hand, substances entering into the makeup of the micro-organism, such as the so-called capsules, resistant ectoplasmatic structures, persistent mucoid envelopes, and the like are involved, then we might hope for an effective immunity with dead bacteria.

Furthermore, if the aggressive activity or virulence of micro-organisms is rapidly lost after isolation from the tissues, the effectiveness of cultures killed by heat, or otherwise, will naturally depend upon the total age of the cultures used, provided the factor of virulence is not completely destroyed when the bacteria are killed. The evident success of the use of heated cultures of typhoid bacilli in preventing an attack of typhoid fever is encouraging for this method of vaccination. Statistics are, however, only to be depended upon when the many errors incidental to such a material

are reduced by large numbers. The fact that cases of typhoid do occur after vaccination cannot militate against the method because great variation in natural resistance to such a disease is known to exist and, as stated before, vaccination is a process governed by quantitative factors. The one serious weakness of statistical evidence in favor of typhoid vaccination is the inevitable entry of sanitary and precautionary and educative influences with vaccination, reducing the chances of exposure as well as the infecting dose.

A new step in vaccination was taken when the vaccinating material, be it living or dead bacteria, was exposed to immune serum before injection. In brief, the bacilli of typhoid fever were loaded, so to speak, with all the immune bodies they would bind and the resulting sensitized bacteria used as vaccine. Even living sensitized typhoid bacilli have been used by Besredka without harm. Gay has shown experimentally on rabbits that the sedimented, sensitized, killed bacteria are preferable to these plus the supernatant fluid in which they are suspended and which is assumed to contain the endotoxins. Swift and Kinsella have recently reported experiments on rabbits with heated streptococci sensitized with a strong antiserum. With non-sensitized vaccine there was strong formation of antibodies (agglutinins, complement-fixing and protective antibodies). In rabbits treated with sensitized vaccines the production of antibodies was low and retarded.

The explanation of such conflicting results following the use of sensitized vaccines may perhaps be found in the behavior of toxin-antitoxin mixtures. In 1907 and 1908 I made a number of observations upon the immunizing effect of such mixtures on guinea-pigs, using accurate quantitative methods in preparing them. It was found that the highest active immunity was obtained if the mixture contained enough surplus toxin to produce a fairly large local lesion, i. e., a mixture which had the effect of $\frac{1}{3}$ to $\frac{1}{2}$ the lethal dose of free toxin. When the quantity of the antitoxin was increased, the toxin remaining constant, the active immunity decreased somewhat. It was still present when the mixture became neutral, i. e., produced no local lesion recognizable in the living animal, but its immunizing properties were extinguished when the antitoxin reached the high level of double the neutralizing dose. The relative efficiency of sensitized vaccines probably depends on a similar quantitative relationship between the antiserum and the bacilli. For diphtheria toxin and anti-toxin this can be accurately

controlled. It is difficult to see, however, just how a similar accurate titration of immune serum and bacteria can be made in terms of any assignable units at present. The only way open is to inject series of mixtures of variously sensitized bacteria and await the result.

The explanation for the very effective immunizing capacities of sensitized toxins I would refer to the greater penetrating power of such mixtures. It is obvious that if we by any means can secure the wide distribution of antibody-producing substances through the various tissues, a co-operative effect will give a better yield than a merely local activity of the antigens. This view of the dispersing effect of sensitization seems supported by the larger number of cases of paralysis in guinea-pigs following the use of diphtheria toxin-antitoxin mixtures than of toxin alone. In other words, the toxin appears to travel farther in combination with the antitoxin than when free. The success of the simultaneous methods of immunization used so widely in the vaccination of animals is probably due to a wider dissemination of the vaccine under the influence of the immune serum, hence a more vigorous production of antibodies.

It is of interest to mention here that Baldwin using the serum of a cow, that had received during a period of ten years six intravenous injections of living human tubercle bacilli, to sensitize tubercle bacilli before injection, found such treated bacilli of greater infective power than those treated with normal cow serum. The reactions came earlier and there was a wider spread of the disease than in the controls. Here also the contradictions seem to me apparent rather than real. If sensitized bacteria have a wider dissemination than non-sensitized, they likewise acquire the capacity to do greater harm if they are virulent enough.

The problems presented by the production of passive immunity with the use of immune serums derived from animals are so well known through the use of diphtheria antitoxin that I need not dwell upon them here. Its advantages following exposure, its limitations because of the transitory character of the protection are shared by all immune sera. It should, however, be borne in mind that the use of such serums during active disease may contribute to active immunity to the extent of introducing the principles of toxin-antitoxin treatment and of the simultaneous method, provided the combinations and proportions of antigen already in the

body and antibody administered are quantitatively favorable to such action. Serums may thus favor or oppose active immunization when used therapeutically.

Perhaps the latest refinement in immunizing methods is the use, not of living or dead virus, but of distinctive parts thereof. Theoretically, the attempt to find the chief antigen of a micro-organism and exclude all others as either unimportant or harmful is just as justifiable as the attempt to immunize the body towards the chief or primary infection and letting the secondary infections alone. The micro-organism may be regarded as made up of various antigens. The living organism is not different from the dead excepting in so far as the production of certain possible antigens is checked and others injured by the killing process. The host does not fight against the life of the pathogenic microbe but only against the products of that life. Of a series of antigens there may be one which represents the primary and therefore the most important aggressive or protective agency of the virus and which, if introduced in abundance as a vaccine, may produce that kind of resistance which later will interfere with the beginnings of the infectious process entirely. The first use of so-called partial antigens is, I believe, to be ascribed to Much, who has derived from the tubercule bacillus protein and lipoid substances for immunization. Even before Much the possible importance of the waxy and fatty substances of tubercle bacilli had been emphasized and tests made by P. A. Levene. Hutyra and Manninger claim to have demonstrated ferments either against the capsules of bacteria or the body substance proper according to which substance was introduced as antigen. Strubell and Böhme found the same kind of partial antigens in staphylococci as in tubercle bacilli. They distinguish staphyloalbumin, staphylolipoids and neutral fats or staphylonastin. Immunization with the staphylococci produced three antibodies, but the lipoid antibodies were less concentrated than after injection of the lipoid antigen.

The study of partial antigens opens a wide field for speculation as well as for difficult and painstaking work. To discover some one ingredient of a micro-organism which can prevent infection with the micro-organism itself would rank with the subtlest discoveries in chemotherapy, for it would at the same time eliminate from the vaccine substances which are injurious and without any useful antigenic properties.

The recent developments in immunological research indicates that medical science is moving away from the doctrine held so long that the toxins or poisons of bacteria were the chief substances against which immunization was to be directed. The most satisfactory therapeutic results with the true antitoxins brought this somewhat artificial situation about originally. The almost universal failure to find some aggressive toxin among the invasive bacteria and the acknowledgment that the toxins found had nothing to do with immunization, as was stated by Neufeld and by Cole for the pneumococcus, should lead to a freer spirit of enquiry, untrammelled by preconceptions as to the functions of toxins. That they are responsible for most of the injury inflicted must be granted, but the injury may be a side issue not in line with the main events. The object of immunization is to suppress the invader. The problem underlying it is to find the precise aggressive weapons which permit the invader to multiply. The capacity of micro-organisms to multiply in the tissues of the host may or may not be due to the direct action of toxins. If not, it would be useless to immunize with them. When we come to treat disease in actual progress, the neutralization of toxins may be a very important therapeutic step, for the body which may be capable of disposing of the micro-organisms eventually by self-immunization may have to be protected against bacterial poisons actually present.

VACCINE TREATMENT.

LUDVIG HEKTOEN, M.D.,

Chicago, Illinois.

My intention is to discuss briefly certain more or less recent developments in connection with vaccine treatment. For this purpose it is not now necessary to review in detail the various stages in the growth of knowledge on which the principles and practice of vaccination, preventive as well as curative, are based. The aim in either case has been to strengthen and to hasten the natural processes that result in protection against infection and in cure of infection.

Curative vaccine treatment, which I shall discuss exclusively, is a direct outgrowth of the increasingly successful prevention of various infectious diseases by means of artificial immunization, and may be said to represent a culmination of the efforts to combat infection with its own weapons, as it rests primarily on the assumption that under certain conditions the production of specific antibodies by the infected organism can be increased with curative results on injection of special preparations of the virus or the bacteria which caused the infection. This conception is in harmony with the accepted interpretation of the preventive action of many bacterial and other vaccines (or antigens) as due to the easily demonstrable formation of new and specific antibodies, which persist for a longer or shorter time, and to the greater readiness, which also is demonstrable in various ways, with which such formation is renewed when the antigen again enters the vaccinated body as may occur in the form of the living germs. Except as tested in Pasteur's experiments on inoculation against rabies after the infection has been received, this explanation of the supposedly curative action of vaccines has not been put to the direct test in animal experiments, largely, it seems, because the animal infections with which we are acquainted are not regarded as suitable for that purpose since they do not appear to duplicate sufficiently the human conditions. Whether the practical results of vaccine treatment for curative purposes support the hypothesis as to the mode of action on which it is based, is even now a debatable question. The

conditions under which vaccine treatment is practised have been allowed to change so much since its formal introduction by Wright in 1902, and have acquired in large degree such character that there are no secure foundations for comprehensive interpretation and final judgment as to the practical value and significance of the results. A hurried review may serve to make this point clearer.

In the early days after Wright's discovery of the opsonins and his advocacy of specific vaccine treatment under the guidance of the opsonic index, much attention was given to this index as a measure of specific resistance (and in less degree as a means of diagnosis). Soon doubts arose as to the value of the index; the accuracy of the method was questioned; and emphasis was put on the limitations of the results as not being a measure of the final degree of immunity because applicable to one factor only, leaving unmeasured other factors equally important and not necessarily subject to parallel fluctuations of activity. The outcome was the abandonment of the index as an essential element in vaccine treatment, which now rapidly passed into general use and, at least in this country, soon became the object of an indiscriminate exploitation, to which the medical profession has offered but little resistance. In a short time various practices were introduced, which are not in harmony either with the conditions demanded by the primary hypothesis or with the teachings of bacteriology and immunology, and which before long reduced vaccine treatment as generally practised from a carefully controlled, essentially scientific procedure to one of guesswork and routine.

The first departure from the course of safety and conservatism was the uncontrolled delegation of the making of vaccines to commercial concerns. According to the fundamental principles, every consideration but that of expediency demands that therapeutic vaccines shall be composed of bacteria as little different and as little removed as possible from the strains causing the infections against which the vaccines are to be used. It is evident that in preparing vaccines on a large scale this condition cannot be met because the changes in virulence and affinities which take place in bacteria under artificial cultivation cannot be avoided. Indeed, there is danger that with time the specific element on which the desired (antigenic) effect depends may be lost altogether. There is the further difficulty that the antibodies evoked by one strain may not act on the other strains of the same species. That this is not placing undue

importance on some remote possibility of no real practical significance is shown conclusively by the regular occurrence of fixed varieties according to antigenic properties in certain species of pathogenic bacteria as illustrated so well by the pneumococcus. So far as we now know, there are no all-inclusive strains of bacteria, causing human infections which might be used to overcome this narrow specificness of immunizing action. In recognition of this drawback to wholesale vaccine-making, the polyvalent vaccine was evolved and made to contain so many strains from different sources that every possibility would seem to have been covered. But after all this is an unsatisfactory substitute for the fresh autogenous vaccine, which, it would seem, offers the best hope that the indications of each case at all times will be met in the most direct way. The principle of using autogenous vaccine as the rule has the further and great advantage that to secure it the definite etiology of the infection must be established—a true etiologic diagnosis must be made and there is an end to guesswork. Undoubtedly the good results obtained by careful scientific physicians who use autogenous vaccines are due in no small degree to the careful study of the patient whereby is disclosed not only the nature of the outstanding infection, but in many cases also hidden bacterial foci that often perhaps are the primary source of the evident localizations and hence require removal before permanent cure can be established.

It was the inability of most physicians to make or have made the bacteriological studies necessary to obtain the etiologic diagnosis coupled with demand for vaccine treatment that paved the way for the commercial vaccine and also for the second, but less excusable and more harmful, departure from the proper course; namely, the acceptance by physicians of the short cut to vaccine treatment without careful diagnosis offered by the ready-made mixed vaccines and by semisecret unstandardizable mixtures of bacterial products. Carried to its logical conclusion, the reasoning that led to these makeshifts would justify the same treatment for all infections, the only diagnosis required being infection. As to semisecret cultural filtrates, no reason can be found to warrant their use as vaccines: their immunogenic values, if they have any, have not been determined; they are not uniform in composition and cannot be standardized; they are more or less toxic, the toxicity being affected by small but uncontrollable differences in the conditions under which bacterial growth takes place. At the same time as commercial

mixed vaccines contain no autogenous elements, there is the further evident objection that there exists no such constancy of bacterial association in mixed infections as would permit the use of ready-made mixtures under the principles of specific vaccine treatment. By accepting the mixed vaccines of commerce the physician abandons reason and begins to grope in the dark, forgetting "that a multitude of remedies is the child of ignorance." His examination of patients tends to become more and more superficial, his diagnosis slipshod, and his treatment routine, without any definite indications and without individualization. If more than one vaccine needs to be given, why not follow the simple and perfectly rational plan of mixing them at the time of injection or of injecting them separately?

As vaccine treatment became readily available by means of stock and mixed vaccines of all kinds, its use was extended to practically all forms of infection, acute and chronic, general and local, and even to conditions clearly not infectious in nature, regardless of whether or not there was any good reason to believe that benefit would come from efforts to stimulate the output of specific antibodies under all these circumstances. As we look back it seems now as if special efforts were made "to hasten the use of the remedy while it still cured." As would be expected, the interpretation of the results often has lacked the discrimination and questioning which accompany the efforts of critical intelligence. The great difficulties in the way of reaching sound conclusions as to the real value of a special therapeutic method, at best with an indirect auxiliary action, in a great variety of infections that are subject to spontaneous improvements and most of which as a rule are spontaneously curable, did not always lead to proper caution in judging the apparent results of the routine and indiscriminate use of vaccines in this large field. The observations have not been always trustworthy or the reasoning just. The simple fact is that we have no reliable evidence to show that vaccines, as commonly used, have the uniformly prompt and specific curative effects proclaimed by optimistic enthusiasts and especially by certain vaccine-makers who manifestly have not been safe guides to principles of rational and successful therapeutics.

While uncertainty and disappointment have developed in regard to the usefulness of vaccines, this must be ascribed perhaps rather more to fault of exploitation than to fault of the thing exploited; for in the original field, restricted to subacute and chronic local

infections under mechanical conditions that are favorable for healing, cautious observers, proceeding as nearly as possible in accord with the principles of immunity, have received the impression that specific vaccine treatment may be of signal value in stimulating the curative resources of the organism. That the beneficial action of specific vaccines in hastening recovery in subacute and chronic localized infections may result from increase of specific antibodies, as assumed, looks altogether reasonable, as the infecting germs may be so enclosed and walled off that specific antigenic elements in adequate quantities do not reach the centers of antibody production. It is of course possible that other and nonspecific factors are concerned in the effects of vaccines, as for example stimulation of the leucocytic activity, which is subject to variation, and liberation of nonspecific ferments, but until recently only scant attention was given to such possibilities. According to this view of the nature of the action of vaccines, acute infectious diseases were regarded as not suitable for vaccine treatment because here the infecting germs, widely distributed in the body, would furnish all the stimulus needed to call forth an abundant supply of antibodies. The original theory of vaccine treatment really furnishes no basis for the application of vaccines to acute infectious diseases, and when, nevertheless, reports were made of good effects from vaccines in acute diseases, such as typhoid fever and pneumonia, we had no preconceived or readily available explanation to offer for the unexpected results. This brings us to the consideration of the remarkable development during the last year or two of vaccine treatment of typhoid fever.

While isolated instances of rapid improvement and even recovery with crisis are and have been ascribed to the injection of specific vaccines and also of semisecret culture filtrates in various infectious diseases, the true significance of such results in most cases remains doubtful on account of the variable spontaneous course of such diseases. But in the case of typhoid fever at least, as I hope to make clear, the situation is different.

Vaccine treatment of typhoid fever was practised first as long ago as in 1893 by Eugene Fraenkel, who gave subcutaneous injections of heated thymus-broth cultures of typhoid bacilli apparently with benefit. It had been found that this vaccine would protect animals against living typhoid bacilli and Fraenkel wanted to determine whether it would modify the clinical picture of typhoid fever when injected during the attack. The method received but little

attention and, save for interesting experiments by Petruschky and by Richardson, it was not until about 1909 that reports began to appear of more or less favorable results from the subcutaneous injections of typhoid vaccines of various kinds. The results while not remarkable were not without encouragement, as the intensity of the symptoms and the duration of the attack seemed to be reduced. In a few cases rather quick cures followed, as had been noted by Fraenkel also. Then came the intravenous injection of the vaccines by Ichikawa (1912) and others with such striking effects as to attract general attention and secure for the method prompt trial at many hands. At present it seems to be the opinion of almost all who have used the intravenous method of injection, that by it the course may be modified and shortened and in a considerable number of cases even cure by crisis produced. As it is very rarely that typhoid ends by spontaneous crisis (according to good authority in about one-tenth of one per cent. of the cases), the occurrence of recovery by crisis in from 30 to 40% after intravenous injection certainly cannot be ascribed to any chance spontaneous cure. The striking immediate results of an effective injection are now well known. Within half an hour or so a chill, often severe, occurs with a rapid rise of the temperature, followed after some hours by a progressive fall, relaxation, profuse perspiration and rapid subjective and general improvement; first the number of leucocytes falls, and then there is a rapid rise to 15000 or more. The subsequent course may be a permanent return to normal temperature and prompt recovery—crisis; a rise of temperature to the previous level and then a gradual fall to normal in a few days—lysis; or the attack may be resumed, running an apparently unmodified or somewhat milder course than before the injection. When the attack is resumed, re-injection after a few days may cut it short, but it appears that if from 2 to 3 injections from 3 to 4 days apart have temporary effect only, no abortive cure need be expected.

Crisis has been produced in typhoid fever by the injection not only of typhoid vaccines of various kinds, but also of colon vaccine, of mouse typhoid vaccine, of meningococcus vaccine, and even albumose. Indeed, the specific nature of Fraenkel's results in 1893 was challenged promptly by Rumpf, who claimed the same results from the injection of products of pyocyaneus bacilli. In infections other than typhoid, nonspecific products injected intravenously may cause acute reactions also, as for example typhoid vaccines in para-

typhoid fever, colon vaccines in puerperal sepsis, pneumococcus and typhoid vaccines in erysipelas,* typhoid vaccines in pneumonia.* In normal persons the intravenous injection of typhoid vaccine may give a reaction much like that in typhoid fever. I may mention, too, that in pneumonia intravenous injection of autolyzed pneumococci, prepared by Rosenow's method, may cause an immediate chill with rise and fall of temperature, and leukopenia followed by leucocytosis, that is, the same general phenomenon as seen in the induced crisis in typhoid, and succeeded in some cases by immediate recovery. In short, the intravenous injection of protein substances may produce a reaction which at least in some respects closely resembles the chills and fever that occur naturally in the course of various infections. We are reminded of reactions observed by Vaughan in his study of protein fever and also of effects said to follow the intravenous injections of certain non-protein substances, gold for instance, in colloidal suspension. Whether the induction of the reaction is associated as frequently with improvement and hastened recovery in other diseases as in typhoid is not known as yet. Typhoid fever is the only disease which has been treated somewhat systematically by the new method and as yet specific vaccines have been used very largely. In their admirable and thorough study of a series of 53 cases of typhoid, treated with Gay's vaccine, Gay and Chickering† found that no permanent benefit resulted in 34%, lysis with shortened course in 24.5%, and critical cure in 41.5%. They report no alarming symptoms from the injections, but others using different methods have reported instances of collapse, of hemorrhage, and of hyperpyrexia with delirium and death, so that this kind of treatment by no means is to be lightly undertaken. Gay would ascribe the good effects to the combined action of specific antibodies and leukocytosis. This view is supported by the facts observed by several that the most pronounced results have been obtained after the tenth day of the disease when the reaction against the infection is fully developed, and that much less effect has been achieved in the incubation period. As the same general results may be produced in typhoid fever by non-specific vaccines and other substances as by various forms of typhoid vaccines, although whether in the same percentages is not known, it is natural that other views should be presented. Jobling

* Unpublished observations by George Mathers and C. W. Wells.

† Arch. Int. Med., 1916, XVII, 303.

and Paterson* find that in animals the intravenous injection of killed bacteria mobilizes nonspecific ferments and they suggest that the effects of specific vaccines and other products in typhoid fever are due to the work of these ferments in destroying bacilli and in reducing toxic substances to non-toxic. It has been suggested also that following the shock of the intravenous injection the organism passes into a refractory condition (antianaphylaxis) in which it ceases to react to the typhoid bacillus and its products. These views, it seems to me, may serve as suggestions for more formal hypotheses to direct investigations for the purpose of learning more of the nature of the reaction and its therapeutic value.

Summary.

If the presentations in this paper are trustworthy, it may be concluded that the general results so far from the routine use of commercial vaccines, polyvalent and mixed, have no value as evidence for or against the curative usefulness of vaccine treatment and hence no value either with respect to the soundness of the theory on which vaccine treatment primarily has been developed.

In subacute and chronic localized infections the results appear to indicate that specific vaccines properly and skilfully used have value, most likely because they increase the production of specific antibodies, as demanded by the theory, but probably also because they stimulate leukocytic and other activities.

In typhoid fever and possibly also in other infectious diseases the intravenous injection of specific vaccines and also of other substances may induce crisis and appear to hasten recovery. The mechanism of this effect is not fully understood, but as it involves something more than or different from specific stimulation of the production of antibodies it can not be interpreted wholly in terms of the current conception of the action of vaccines. We appear to be entering, therefore, a new and interesting development in the study and treatment of infectious diseases.

* Jour. Am. Med. Assoc., 1916, LXV, 515.

THE PRACTICAL APPLICATIONS OF SERUM THERAPY.

WILLIAM H. PARK, M.D.,

New York City.

The advisability of using sera in any particular disease is influenced by a number of considerations. The primary one is whether a serum has been obtained and is available which contains antibodies of suitable kind and amount to neutralize the toxins or aid the body cells and ferments in destroying the micro-organisms. Others almost equally important are whether the infections can be identified from clinical signs alone, or only after additional laboratory examinations, and whether the sera can be brought into contact with the toxin or organisms at the essential points, in the necessary concentration and within the required time. Practical Serum Therapeutics in the more important infections in which some results have been obtained will be considered in the light of the above considerations.

Serum Treatment of Lobar Pneumonia.

This disease is so uniformly due to one organism that from the clinical signs alone, the physician can almost assume a pneumococcus infection. This knowledge is not as valuable as it seems since it has become evident that the characteristics which define a pathogenic micro-organism are frequently so broad as to include a number of strains, which from the viewpoint of immune sera, are types as distinct as micro-organisms with wide cultural difference. The term "pneumococcus" as pointed out by Neufeld is one of these broad group names which cover a number of strains each one of which is unaffected by the antibodies produced through immunizing injections with the others.

A further extremely important differentiation between the types is that with our present methods some excite by their injection into suitable animals abundant antibodies, while others do not. The reasons for this we do not understand. The most recent and most thorough investigation concerning the value of the specific serum for pneumonias due to each type of organism has been carried on

at the Rockefeller Institute for Infectious Diseases by Cole and his associates and the present favorable outlook for treating a certain proportion of pneumonia cases is largely due to their work.

Cole judges from the examinations made by him and by those working in coöperation with him, that in the United States about 75 per cent. of all lobar pneumonia cases are caused by pneumococci of three types which are numbered I, II and III. The other 25 per cent. are caused by a multitude of strains so numerous that in a moderate number of cases no repetition of the same type is apt to be met with. For convenience these different strains are grouped together as type IV. When horses are treated by our present methods with repeated intravenous injections of types I, or II or III, it is found that abundant immune bodies develop in response to I, only to about 10 per cent. of the extent to II and still less to III. Some of the pneumococci group under type IV produce antibodies while others act like type III. The strength in protective bodies is measured by injecting mice with a definite dose of virulent pneumococci together with a definite amount of serum.

The identification of the pneumococcus is made by injecting the fresh sputum into the peritoneal cavity of a mouse and after 6 to 12 hours, washing out the peritoneal cavity and testing the agglutinating characteristics of the greatly multiplied pneumococci. Contaminating bacteria generally lessen in number rather than increase.

This test is usually successful in the hands of experienced workers and requires 8 to 14 hours for its completion. The test in the hands of those who are inexperienced is apt to fail entirely. Several mice should be injected from each specimen to insure a successful result.

Cole's, Longcope's and Richardson's statistics of the frequency and the mortality of pneumonics due to the types are of great practical interest.

	Number		Per cent. Incidence		P. H. Per cent. Mortality		Un. Penn. Hospital, Richardson.		
	Cole.	Longcope.	Cole.	Longcope.	Cole.	Longcope.	No.	Per cent. Incidence	Per cent. Mortality
I	78	*(13)	33	*(23)	25.0	*(12.5)	60	31	30
II	75	(11)	32	(21)	29.0	(72.7)	39	20	25
III	22	(7)	9	(14)	45.0	(85.7)	13	6	50
IV	48	(21)	20	(40)	12.5	(23.8)	83	43	12
Other bac.	14		6						

It is noticed that about 30 per cent. of the cases of pneumonia and about one third of the total deaths are caused by infections with type I.

* Presbyterian Hospital, Longcope.

These figures are very important because at present the results of serum injections follow their antibody content and seem favorable in type I infections, doubtful in type II and absolutely negative in type III and in type IV.

Method of Administration.

The experimental work in animals and the observation of cases has led to the general use of larger injections and the substitution of the intravenous for the subcutaneous method. The size of the patient and the strength of the serum in antibodies have not been considered in controlling the size of the dose, although all accept the fact that theoretically they should. The serum should be standardized, as in the case of antitoxins, 0.2 c.c. of a recent serum should protect against 100,000 f. d. of a very virulent number I type of pneumococcus and serum should seldom be put out or used that contains less than half this strength.

Cole advises that 80 c. c. of serum diluted with 80 c. c. of salt solution be injected intravenously and repeated about every twelve hours till permanent improvement is noted. Usually he gives three to five doses.

The repetition of the dose every twelve hours is founded not so much on scientific observation as on the desire to give it surely sufficiently often. In our own experimental work, we have found that a single dose of 0.1 c. c. protects a mouse for the next four days from an injection of 1,000 fatal doses of living pneumococci, and as late as the 15th day, from 100 fatal doses. This suggests that somewhat less frequent injections may be sufficient.

In order that comparative results should be obtained, it is necessary to have all antipneumococcic sera labelled as to the strength and nature of antibodies and the date of the last potency test. The serum used should have been tested within three months, for it gradually deteriorates.

Cole recommends that the serum be only given in a case after the bacteriologic test has shown the type. I believe, in severe cases a first dose of type I serum should be given as soon as possible and the later injections only after the bacteriologic report. Outside of hospitals Cole's plan means in most cases a delay of at least twenty-four hours and generally prevents the use of serum altogether.

It is understood that the severe cases which receive an injection of type I serum and from which no bacteriological report is

received cannot be considered as having any value in forming an opinion of the effect of the treatment; thus if Dr. Longcope had treated all his cases with type I serum and had not identified the infecting type in each of the 22 deaths among his 52 patients he could have had no conception of the value of the serum, for only one of the deaths and 13 of the cases were due to the type I organism.

The fact that such really promising results have been obtained in cases due to type I leads us to hope that Wadsworth, Cole and others will succeed in their endeavors to get a therapeutically valuable serum for types II and III, and possibly so concentrate the antibodies as to use a combined polyvalent serum.

The results of large intravenous injections of specific serum in type I infections.

There is in about 30 per cent. of the cases an almost immediate more or less severe chill with a considerable rise of temperature which lasts for a short period. This occurs usually after the first but sometimes after the later serum injections. If the blood contained pneumococci, they disappear within 12 hours after the injection. The temperature usually rapidly falls after the initial rise to a point lower than before the rise and the symptoms, as a rule, improve sooner than the average untreated case of equal severity. The mortality up to the present time has been much less than in the untreated cases. Serum sickness with rashes, painful joints, swelling of lymph glands and other symptoms occur to a greater or less extent in about 50 per cent. of the cases during convalescence. The serum sickness, while it lasts, is very annoying, but not dangerous.

Serum Treatment of Epidemic Meningitis.

The intraspinal method of injecting serum from horses immunized to meningococci in meningitis introduced by Jochmann has been approved by all. The collective investigation carried out under Flexner's supervision settled for all its value, and if it were not for the somewhat discouraging reports lately received from England it would not be necessary to more than allude to the value of the serum.

Several reports from England mention a mortality under serum treatment of different collections of cases of from 52 to 63 per cent. and several experienced men have advised against the use of the serum.

Should these results in any way cause us to change our favorable opinion?

There are undoubtedly certain epidemics in which an unusual proportion of the cases develop a thick tenacious exudate which greatly hinders the successful use of the serum. A number of these have been met with at the New York State Quarantine Station. Again, the sudden great foreign demand for the serum caught some of the manufacturers with a small supply and the attempt to replenish their stock caused them to bleed their horses too frequently and thus obtain a serum which was found at a later period to be poor in antibody content. Unless the strains used are properly selected the antibodies may not be suitable to combine with the strain producing the local epidemic.

That one or more of these explanations for most of the poor results are probably true is rendered more probable by the fact that Robb, who has had a very large experience in a previous epidemic, had, using a potent serum, a mortality of only 36 per cent. in the same outbreak. Since 1910 the New York City Health Department laboratory has treated all cases of epidemic meningitis applying to it. Our mortality in 1914 was 26 per cent., and last year 34 per cent. Our results are thus similar to those of Robb. Drs. Sophian, DuBois and Neal, who have had charge of the serum treatment for the laboratory, are absolutely convinced of the value of the treatment, not only from the clinical course but from the changes which take place in the spinal fluid as shown by the disappearance of the meningococci.

Administration of the Serum.—Dr. Neal finds that too often the private physician fails to repeat the injections sufficiently often. It is very rare, except in a case already convalescent, that it is correct to give daily injections for less than four days. If the organisms or symptoms do not disappear the injections of 10 to 25 c. c. of serum should be continued for many days. Fortunately lumbar puncture with removal of fluid is of value in the treatment. Unlike pneumonia, practically all cases of epidemic meningitis can be treated by a single polyvalent serum. The different strains do, indeed, differ, but they have group relationships and intravenous injections of suitably selected strains cause the horse to produce a serum capable of influencing almost all strains. This has been recently carefully investigated by Dr. Wollstein at the Rockefeller Institute. It should be insisted upon that every lot of serum be

tested for its complement fixing, opsonic and agglutinating power until at least some better method be devised to estimate its value, and the results of the tests should be stated on the package. An agreement should be reached to make a standard unit. The fluid removed from every case of suspected epidemic meningitis should be examined microscopically, for in this way only can a correct diagnosis be made.

Antistreptococcic Sera.

The same reasoning applies as with the antipneumococcic sera and the same dosage and method of administration.

Some of the strains recur frequently, others infrequently in infections. If we suspect that the infection is with the hæmolytic type we can rightly give this type of serum with the hope of some good resulting.

If we suspect the veridans type we give a polyvalent serum of this type with less prospect of help.

The organism should be identified as soon as possible and if virulent in mice tested against the serum in a mouse. Much further combined clinical and laboratory investigation is required before a decision can be arrived at as to the value of the serum and the best dosage.

If it were not for the serum sickness there would be no question that the injections should be made early before the infection has advanced and the streptococci acquired a somewhat greater resistance to the distinctive effect of the serum antibodies and ferments.

The repeated local bathing of exposed infected tissues with the serum seems to have a beneficial result beyond that exercised by a non-specific serum.

The Serum Treatment of Dysentery.

The earlier opinion has been confirmed that bacillary dysentery alone occurs in cold and temperate climates while in hot climates both bacillary and amebic cases occur about equally. The idea that summer diarrhœas were frequently due to the dysentery bacilli has been discarded. The bacilli may be present at times in small numbers in these cases, but they have too little part in the disease process to require specific treatment. Like so many other bacteria causing inflammations of mucous membranes, the organisms exciting dysentery belong to a variety of strains.

Shiga discovered the first strain and as this is the most widespread and probably the most toxic, it seems well to call this the dysentery bacillus and the others paradysentery bacilli. The most important of these in the United States are the strains isolated by Flexner, Hiss, Park and Strong. These are separated by their action on sugars and by complement fixation and agglutination tests. The serum produced by one is only feebly active on any of the other strains. For sporadic cases and those occurring in the beginning of an outbreak, a polyvalent serum should be used. In an epidemic where the strain has been identified the monovalent serum is to be used if possible.

The serum in mild cases is given subcutaneously in doses of from 10 to 30 c. c. twice daily according to the size of the person. In severe cases as high as 100 c. c. two or three times in the twenty-four hours can be given, and in desperate cases the serum has been given intravenously. If given intravenously, the serum must be warmed and given slowly. The doses are to be continued from day to day until permanent improvement is established. Injections are usually continued for two or three days. The majority of those who have used the serum confirm Shiga's original belief that the results are good. My own experience in a number of severe cases is on the whole favorable. I believe it is unnecessary to use the serum in slight cases. In favorable cases within six to twelve hours the constitutional symptoms frequently improve. There is at this time some reduction in the number of stools though they may be more copious and have increased sloughs. The serum on the market is not standardized and some of it is valueless. The necessity of using a polyvalent serum in most cases also lessens its value. In spite of these objections the use of the serum in severe cases is strongly indicated. It is very desirable that records be kept of the cases treated and that results be reported.

Shiga believes the mortality to be reduced by the serum treatment from around 35 per cent. to about 9 per cent. Some report even more striking results, while still others have met with disappointment. Undoubtedly the extent of mixed infections with other organisms, the possibility of some cases having been due to ameba and the use of inactive serum must be considered as being possibly the cause of the failure of the serum in these cases. Ruffer and Willmore showed that the Shiga type of serum had no effect

on their cases which were due to T or Y type of paradysentery bacillus. Either a polyvalent serum or a suitable monovalent serum was found effective.

Convalescent and Normal Human Serum.

The serum or whole blood is used for two reasons. The possible value of antibodies that may be present and the nutrition given. The fact of its being human blood is an advantage.

Scarlet Fever.—Convalescent serum or whole convalescent blood has been used in the treatment of early toxic cases of scarlet fever both here and abroad and has given encouraging results in the limited number of cases observed thus far. Reiss and Jungman recommended the intravenous injection of 50 to 100 c. c. of pooled and convalescent serum, while Zingher makes use of the intramuscular injection of whole convalescent blood, citrated or noncitrated, which he injects in quantities of 120 to 240 c. c. The blood causes no local inflammatory reactions in the muscles, and is rapidly absorbed. The convalescent serum or fresh whole blood is obtained from patients who are 2 to 3 weeks convalescent from scarlet fever. These donors should be free from syphilis and tuberculosis.

The effect of convalescent serum or whole blood in the uncomplicated early toxic cases of scarlet fever is seen in a critical drop in temperature, beginning about 6 hours after the injection and ending in from 24 to 36 hours; an early fading of the rash; improvement in the circulation and character of the pulse; and especially in the general condition and mental symptoms of the patient. Zingher reported the results obtained at the Willard Parker Hospital with intramuscular injections of whole convalescent blood in 15 very toxic cases of scarlet fever, selected out of a total of 900 admissions. A striking effect was noted in 5 cases, improvement and final recovery in 6 more, while 4 patients died from various septic complications.

In the later septic cases, seen from 5th to 10th day of disease, complicated by an extensive streptococcus exudate over fauces and tonsils, enlarged and tender cervical glands, a poor circulation and showing general septic temperature, fresh normal or convalescent blood, injected in quantities of 120 to 240 c. c. and repeated if necessary in 3 to 4 days has shown beneficial effects in some des-

perately ill cases. Fresh normal blood probably has no specific action in septic cases of scarlet fever, but it supplies definite nutritive, stimulating, and normal bactericidal substances.

Infantile Paralysis.—The intraspinal injection of 10 to 15 c. c. of human serum from recovered cases has been advocated by Netter. The excessive spinal fluid is first withdrawn. He reports favorable results. Levaditi and Flexner showed that the intraspinal injection of immune serum in monkeys shortly after the introduction of the virus would prevent an otherwise certain infection. Given at the time symptoms appeared it was powerless. The injection of the serum is apt to be followed by some increase in the symptoms due to meningeal irritation and by a temporary rise in temperature. I have had no personal experience in the use of the serum, but the evidence indicates that it should be tried on a larger scale.

Anemia, Toxemia, etc.—Fresh whole blood, injected intramuscularly in quantities of 100 to 300 c. c., can also be used in acute and chronic exhausting diseases where the nutritive and bactericidal value of homologous protein is distinctly indicated. Cases of acute and infectious diseases, certain forms of anemias, malnutrition of infants, chronic forms of sepsis and various toxemias will be benefited by the treatment. The hemostatic action of fresh whole blood can also be utilized in cases of hemorphilic, purpura hemorrhagica and hemorrhage from various causes, such as metorrhagia, renal and intestinal oozing and post operative hemorrhage.

Administration of Tetanus Antitoxin for Prevention and Treatment.

Prevention.—An injection of 1,000 units insures protection from infection of tetanus for at least ten days and usually for several weeks. If, at the end of ten days, the condition of the wound is such that continued infection is feared, a second injection should be given and, under very unusual conditions, a third. The results following such immunization have been excellent; the fear of tetanus being practically removed. Antitoxin on an enormous scale has been used in the immunization of the wounded in the present war. The New York City Department of Health Laboratories alone have already contributed enough for 200,000 men.

Treatment.—While tetanus antitoxin has proved most efficacious in the prevention of tetanus, its employment as a curative agent has been much less successful, and the opinion of those who

have used it as to its value is most varied, many even doubting its worth. This failure to produce more uniformly good results is chiefly due to its late administration, insufficient dosage and the use of the subcutaneous or intravenous methods. While the subcutaneous use of antitoxin, which at first was the usual method employed, may prove of some value in large doses given within the first few hours after the onset of symptoms, nevertheless, it usually fails because of slow absorption and the time required to reach the tissues of the central nervous system. The intravenous method overcomes the fault of the slow absorption, but not that of the difficulty of reaching the toxin in contact with nerve cells. The intravenous method, while far in advance of the subcutaneous one, is far inferior to the intraspinal injection. In the light of our present knowledge, even the intravenous method when used alone can be justified only by an inability of the physician, for one reason or another, to give an intraspinal injection. The latter method is being more and more recommended, and when employed before the disease has made too much headway has given surprisingly good results. Practically no other method is now used in New York City. This change has come about in the following way.

From time to time since 1903, single cases or small series of cases have been reported in which the antitoxin has been given intraspinally or into the ventricles. Thus Neugebauer* in 1905 reported forty-three cases from Continental and American sources with a mortality of twenty-two or 51 per cent., and also three patients treated by himself of whom two recovered. Abbe and Rogers reported its use in several cases in New York City. Many of these patients received also intravenous or subcutaneous injections or both. The results seemed to the observers to be better than when other methods were used. The cases were too few, however, to convince either themselves or others so that this method of treatment did not become generally adopted. Experimental proof of the greater value of the intraspinal method has not, until very recently, been available. Permin of Copenhagen, working on rabbits and dogs, showed that local tetanus could be prevented by the simultaneous injection of tetanus toxin intramuscularly and a dose of antitoxin given in the spinal canal, whereas with the same dose of antitoxin given intravenously, local tetanus occurred. Four

* Neugebauer; Wiener klin. Wchnschr., 1905, XVIII, 450.

hours after the giving of a large dose of toxin neither method of preventing the occurrence of local tetanus was efficacious, and when nine hours were allowed to elapse between the giving of toxin and antitoxin, the animals could not be saved.

A series of experiments by Dr. Nicoll and myself with guinea pigs were undertaken with the object of determining to what extent tetanus antitoxin injected in the spinal canal has greater curative power, when the disease is actually established, than when given in the circulation. The results were conclusive in showing that the intraspinal injections frequently save life when all other methods of giving serum fail. We made four separate tests and in every one the result was the same. The protocols for the last one of these are as follows:

Experiment 4.—March 24, eighteen pigs were injected into the hind leg with two minimal fatal doses of toxin proportioned to the body-weight of each. Twelve of these were given antitoxin in the amount and by the methods indicated, seventeen and one-half to eighteen hours later, the inoculated leg being stiff in the degree noted at the time. The remaining six were held for twenty-two and one-half to twenty-three hours after inoculation, as the stiffness was not marked until that time.

TABLE.—ADMINISTRATION AND RESULT OF ANTITOXIN IN EXPERIMENT 4.

No.	Weight gm.	Cond. of Leg	Method	Amount units	Result
116	290	Fairly stiff	Control	...	D 3 days
42	310	Fairly stiff	Control	...	D 3 days
296	250	Slightly stiff	H.	100	D 8 days
227	275	Fairly stiff	H.	100	D 4 days
399	300	Fairly stiff	H.	100	D 5 days
316	255	Slightly stiff	N.	200	D 4 days
287	255	Fairly stiff	N.	200	D 3 days
289	280	Fairly stiff	N.	200	D 3 days
306	285	Slightly stiff	N.	200	D 3 days
59	255	Stiff	Sp.	10	Discharged April 23; normal
304	275	Fairly stiff	Sp.	10	Discharged April 23; drags leg
321	320	Fairly stiff	Sp.	10	Discharged April 23; drags leg

Six Given Antitoxin 22½ to 23 Hours after Inoculation

102	300	Stiff	H.	100	D 5 days
10	325	Stiff	H.	200	D 4 days
272	350	Stiff	H.	200	D 4 days
263	285	Stiff	Sp.	50	Discharged April 23; drags leg
123	325	Stiff	Sp.	50	D 5 days
294	350	Stiff	Sp.	50	Discharged April 23; drags leg

Protocols.

The results obtained in the four tests seemed to us absolutely conclusive of the superiority of the intraspinal method of giving antitoxin over the intravenous method as well as all others. It will be noted that in the fourth test only those animals receiving the antitoxin in the spinal canal were able to survive. This result is the more striking since the amount of antitoxin given them was only a fractional part of that given in the circulation. The attempt made to give the antitoxin to four guinea pigs intraneurally was not altogether successful. Under an anesthetic the sciatic nerve of the affected limb was cut down on and freed from the surrounding tissues, as much antitoxin as could be introduced into the nerve sheath injected, and the remainder intramuscularly directly along the course of the nerve. Owing to the small caliber of the nerve, most of the antitoxin passed to the deep intramuscular tissues. The animals lived no longer than those receiving subcutaneous injections.

Cases Treated by Intraspinal Injections.—We have treated up to the present time 20 persons; of these 16 lived and 4 died. The following two characteristic cases present one that recovered and one that died.

Case 15.—L. M., male, aged 18 years, was admitted to St. Peter's Hospital, March 27, 1915, with a crushed and lacerated wound of the great toe. The wound was immediately disinfected and properly dressed. March 30, the tip of the toe sloughed off. *April 6th, the patient had a severe chill and complained of sore throat. There was noted a slight stiffness of the jaw. In the afternoon there were marked stiffness of the back, and occasional slight convulsions when the patient was disturbed. Twenty thousand units of tetanus antitoxin were given intraspinally four hours after the occurrence of the chill. On the 7th, the symptoms increased in severity, convulsions*

occurring on the slightest irritation. There were marked opisthotonos and rigidity. Ten thousand units of antitoxin were given intraspinally under an anesthetic. On the 8th, the patient's condition was about the same. Ten thousand units of antitoxin were given intravenously. *After the tenth day, the convulsions stopped;* the rigidity continued some time longer. April 22, the patient was up and about with slight rigidity. He was discharged cured a few days later. The quantity of antitoxin given was greater than required.

Case 19.—E. C., boy, aged 13 years, admitted to Bellevue Hospital, June 30, 1914, fourteen days previously had fallen and cut his head. *Eleven days later he had abdominal pains and vomiting, which were regarded as due to appendicitis. On admission to the hospital he had marked opisthotonos, locked jaws and inability to swallow. A convulsion occurred on the slightest disturbance. He received 10,000 units of antitoxin intraspinally and 10,000 units intramuscularly.* The patient's condition grew worse from the time of his admission and *he died within twenty-four hours.* The disease had evidently progressed too far to be influenced by antitoxin.

Human Serum.

Dosage Recommended.—Our present practice is to give as soon as possible 5,000 to 10,000 units of antitoxin intraspinally and 5,000 to 10,000 intravenously. We repeat the intraspinal injections after 24 and 48 hours.

The Administration of Diphtheria Antitoxin, Prevention and Treatment.

Prevention of Diphtheria.—The value of an injection of 500 to 1,000 units of antitoxin is now an accepted fact. The period of complete immunity is in different individuals from 12 to 30 days. A repetition of the injection confers an added immunity of only about 6 to 15 days on account of the quicker elimination of the antitoxin in persons sensitized to horse serum. The use of the Schick test and the toxin-antitoxin mixtures are gradually curtailing the immunizing use of the serum to susceptible persons. Under my direction Dr. Zingher and his colleagues in the Research Laboratory have injected over 10,000 persons with the Schick test. Our results have corroborated in every way Schick findings. About 65 per cent. of the younger children were found to be immune

and about 80 per cent. of adults. We now only give immunizing injections to those in the contagious disease hospitals, who show a positive reaction. We are beginning to apply the Schick test in all institutions and hope to do so in the primary schools. We have found that once a child develops natural immunity to diphtheria that this is a permanent condition. Children having cards showing they have had a negative test are considered safe even if exposed to diphtheria or carriers.

The use of the toxin-antitoxin mixtures in institutions is giving us encouraging results. Three injections are given to each person. Over 90 per cent. of susceptible persons have developed immunity within ninety days after the treatment. This immunity is quite lasting. The cases have been followed for over one year.

TREATMENT.—Although more than twenty years have elapsed since the introduction of diphtheria antitoxin in the treatment of diphtheria, good observers, although nearer together than at first, still differ in the amount which they believe should be injected and in the method of its administration. Before giving our own conclusions on the proper dosage, it is well to consider several important points upon which this dosage is founded.

The amount of toxin in any case of diphtheria is comparatively small. One hundred units of antitoxin which would neutralize fifty times the amount of toxin sufficient to kill a six-year old child, would surely make harmless all the toxin present in the most malignant cases if it could gain access to it in time. If we gave antitoxin, therefore, as many suppose simply in sufficient amount to neutralize the poison in the body of an infected person, comparatively small amounts would be injected, but we have to give very much more than this because of the time it requires for much of the antitoxin to reach the toxin. This can be brought into direct contact with the toxin only by being absorbed into the blood and then passing through the capillary walls to the tissue fluids and cells. The greater the quantity of antitoxin that is in the blood, the greater will be the speed that an appreciable amount will pass to the tissues. The combined endeavor of the clinical observer and the laboratory worker is to find the suitable dose which will give a sufficient concentration in the blood to neutralize, as quickly as necessary, the toxin in the tissues. In the laboratory, we can test the amount of antitoxin which is absorbed into the blood from any given dose and the amount which passes out to the tissues, while the clinical

observer can note the changes which take place as he watches the case after antitoxin treatment.

It is naturally a matter of great importance as to how the antitoxin is administered. When given subcutaneously, the swelling caused by its injection rapidly disappears from the absorption of the water, but the globulins and antitoxin remain behind in the tissues because of the slow absorption of proteins. By testing many patients, it has been found that it takes 24 hours for the major part of the antitoxin to be absorbed by the blood from the subcutaneous tissues and some 12 hours from the muscles. For its total absorption it requires two or three days. Through the use of the Schick test, it has been determined that an injection of antitoxin given intravenously passes out to the tissue fluids about ten times as rapidly as when the dose is given subcutaneously and four times as when given intramuscularly. A unit gives most effect when given intravenously and least when given subcutaneously. If it were not for the fact that it is more difficult to give it intravenously and also that sharper serum reactions occur, the intravenous method would be the only one used. Another matter which is of importance is the size of the individual treated. It is self-evident that, if a child weighing twenty pounds is injected with 10,000 units, it would, on the average, have in its blood five times as much antitoxin per cubic centimeter as a person receiving the same amount who weighs 100 pounds. The influence of weight on the dose is, however, largely neutralized by the fact that diphtheria in the child is generally more dangerous than in the adult. Every minute of delay in the neutralization of the toxin in a severe case is of importance, but in a mild case, where dangerous poisoning is still remote, slight delay makes little difference. Infants and children are especially liable to laryngeal diphtheria, so that every case in a child presents a certain gravity which the adult does not present.

The last point to be considered is as to whether a single or a multiple dose should be given. It must be realized that antitoxin has no effect whatever on injury which has already taken place. It is as useless as water on the ashes of a burned-out building. If the toxin is permanently united with the cell substance, antitoxin is no longer of any service. It is the early and sufficient dose which is important. When we give a divided dose, we simply get the effect of the first portion during the interval before the giving of the second dose. If the second dose had been given with the first, we

would have had its effect added, and so an insufficient dose made adequate. When the first dose has been of a sufficient size, the second and third injection, though harmless, are absolutely useless. The holding back of a part of the first dose so as to give it later, simply delays its action to a time when it cannot have much, if any, effect.

For the last three years, we have used in the hospitals for contagious diseases only a single dose of antitoxin, which in mild cases has been given subcutaneously; in moderate cases subcutaneously or intramuscularly; and in severe cases, intravenously or intravenously and intramuscularly. After twenty years of experience in treatment and animal experimentation and consultation with physicians in New York and elsewhere, the following dosage, which is that adopted by the Health Department of the city and state of New York, is advised:

Dosage of Units of Antitoxin in Diphtheria

Single Dose Only

Mild	Moderate	Severe	Malignant
	Infant, 10 to 30 lbs. (under 2 years)		
2,000	3,000	5,000	
3,000	5,000	10,000	10,000
	Child, 30 to 90 lbs. (under 15 years)		
3,000	4,000	10,000	10,000
4,000	10,000	15,000	20,000
	Adults, 90 lbs. and over		
3,000	5,000	10,000	15,000
5,000	10,000	20,000	40,000

Method of Administration

Subcutaneous or Intramuscular	Intramuscular or Subcutaneous	Intramuscular or ½ Intravenous and ½ Intramuscular or Subcutaneous	½ Intravenous and ½ Intramuscular or Subcutaneous

The above amounts are large and not small, and I think no appreciable advantage would be obtained by increasing them. Very much smaller doses are still able to do great good as the general blood current soon becomes antitoxic and blocks any further passage of toxin from the diseased tissues to other portions of the body. The feebly antitoxic plasma gradually permeates the body. There will be, however, more delay in the improvement of the local process,

for the neutralization of the concentrated toxin in the diseased tissues will be slower. The exudate or pseudo-membrane will continue to increase for some hours after the complete neutralization of the toxin because the injury to the tissue cells takes time to manifest itself.

It is necessary in each case to weigh the indications for the different methods.

The disadvantages of the intravenous method are, first the difficulty in giving the serum in small children and infants. In these, it is necessary to inject it directly into the jugular vein or do a cutting operation to render a vein accessible. The injection, here, requires experience and dexterity and sometimes meets with objections from the side of the family or friends.

The second disadvantage is, that the injection of the serum, even though it is warmed and given slowly, is apt to be followed in from 15 minutes to 1 hour, by a rise of temperature and a chill. In about 40% of the cases, a moderate or severe chill will take place which lasts for from five minutes to one hour. With this the temperature may rise from 2 to 5° F. Within a few hours the temperature falls to its previous level or below and no bad effects are noticeable. The serum reaction may be disturbing at the time and impresses unfavorably, not only the family, but also the physician.

There is no doubt that in cases which have already been sick for from 24 to 72 hours and which show a great extent of disease as shown by, locally, the amount of pseudo-membrane and of swelling and constitutionally by symptoms due to toxic absorption, that every minute's delay in getting the antitoxin to all parts of the body is serious, and that in these, an injection of 5,000 to 10,000 units of antitoxin intravenously is imperative.

On the other hand, the mild and moderate cases of diphtheria are not, as a rule, toxic when admitted and here a subcutaneous or, better, intramuscular injection is sufficient. It is true that an intravenous injection would produce a quicker local effect, but the difficulty of administration and the more serious serum reaction more than counterbalance this.

The decision in the laryngeal cases is difficult. Some years ago, in coöperation with Dr. Raymond B. Mixsell, we treated 158 cases of laryngeal diphtheria in a manner that every other case got an intravenous injection and every other one a subcutaneous injection. The results were rather surprising in that, while those injected

intravenously showed a quicker response, the death rate was apparently unaltered. The serum reactions were also not marked.

The results can be summarized as follows:

If we calculate the total death rate of the series, irrespective of the occurrence of broncho-pneumonia, we have the following figures:

	Cases	Deaths	Per cent. of Mortality
Intravenous	79	36	45.5%
Subcutaneous	79	42	53.1%
Totals	158	78	49.3%

The mortality percentages show an apparent advantage in favor of the intravenous method.

Upon examining the records, however, this implies little. The most startling thing is the prevalence and almost absolute mortality of broncho-pneumonia. 45.5% of the intravenous series, and 51.9% of the subcutaneous series developed broncho-pneumonia either before, or a day or two after admission. Out of a total of 77 cases of broncho-pneumonia only 5 recovered, making a death rate of 93.5% for the broncho-pneumonia cases in both series. Of the subcutaneous cases developing broncho-pneumonia 93.5% died. Of the intravenous cases developing broncho-pneumonia 88.8% died.

If we exclude the pneumonia cases, the mortality goes down at once. This is a total rate of 7.4% for 81 cases not developing broncho-pneumonia.

Discussion.

Dr. Frank Billings (Chicago): I shall confine my remarks to a discussion of the question of vaccines. I shall not discuss the prophylactic use of vaccines, for that question has a scientific basis and the practical usefulness of preventive vaccination, though limited, has been proven. What I wish to say will be limited to vaccine therapy, in acute diseases and more especially in chronic disorders, based upon my own clinical experience.

In the use of vaccines consisting of bacteria, killed by heat or by chemicals, we have had the critical advice of L. Hektoen, H. Gideon Wells and others, and the aid of E. C. Rosenow, D. J. Davis and others. We have attempted always to use autogenous vaccines,

by making a bacterial diagnosis of each individual. The bacterial diagnosis is not always readily made. We have made cultures of the blood, infected tissues both focal and systemic and have injected animals intravenously to ascertain the pathogenicity, tissue tropism and specific factors of the isolated bacteria. This we have been able to do in a large clinical material, with the willing coöperation of patients by the removal of tissue of the primary focus, and of exudates of serous cavities, lymph nodes, bits of muscle and other systemic tissues in chronic diseases, especially of patients suffering from chronic arthritis. As nearly as possible, therefore, the autogenous vaccine represented the bacteria exciting the morbid changes in the patient. We also attempted to estimate the results of the vaccination by a study of the opsonic index and also the phagocytic index of each patient. This involved much time and labor and after two years was abandoned as both untrustworthy and impractical. The local, focal and constitutional reactions of the patient, to the vaccines, in various doses, were also studied. These reactions were so varied in many patients that deductions could not be made from them. Many patients thought they felt more comfortable, others complained of greater suffering after vaccination. The local skin reaction, at the point of inoculation, was never constant after the second or third vaccination. Focal reaction was never objective and constitutional reaction as manifested by increase of temperature was practically always absent. We also used vaccines sensitized with serum of a horse immunized with polyvalent strains of streptococci,—chiefly the green color producing strains. Unvaccinated patients were observed as controls. Accurate records were kept. Recently we have tabulated over 500 patients suffering from chronic infectious arthritis, who have been carefully studied and managed. The majority received vaccines. Patients suffering with chronic pyelitis, furunculosis, chronic infectious (streptococcus viridans) endocarditis, pyorrhoea alveolaris and other chronic diseases have received autogenous vaccines. The improvement in any of the conditions named was quite as often negative as positive and the good results could be ascribed, as shown in the controls, by the other measures of management. Theobold Smith and Richard M. Pearce have clearly defined the limitations of the use of vaccines therapeutically, and have also shown the difficulties of a rational choice of a specific vaccine in both acute and chronic disease. We know that the presence in the body of pathogenic bacteria will arouse the

defenses of the host against the invaders. We know that undue exposure to cold, fatigue, lack of nourishment, senility and other factors will lower the protective powers of the body. Consequently the removal of all of these factors, as nearly as may be by management, will help to restore the natural defenses and aid in the destruction of the diseases producing bacteria. My experience is that a personal and general hygienic management will accomplish quite as much without as with vaccines and that vaccines without proper attention to a hygienic management is more likely to be harmful than helpful. Furthermore, autogenous or other vaccines, used to overcome a local undrained infection, will usually have no result. Thus pyelitis, associated with morbid anatomical conditions of the urinary tract, which favors urinary stasis, will not yield to vaccines. A furuncle if incised and drained may quickly heal, but may last many days under vaccine treatment alone. The craze for vaccines has made many physicians lose sight of the principles of the etiologic, constitutional factors, which promote infection and which must be modified or relieved as a chief part of the management. My experience, of several years, in the use of autogenous vaccines, in chronic infectious diseases, justifies the statement that the results do not justify their use. This final judgment necessarily implies some exceptions, but not more than would be the rule in other forms of therapy.

The use of vaccines in the acute infectious diseases has not been followed by results which encourage their use by the clinician. When used subcutaneously the result has been uncertain, variable and paradoxical as shown by clinical reports. Recently the use of bacterial vaccines and other protein substances, intravenously, seems to show a non-specific, uniform reaction, manifested by chill, high fever and physical discomfort, followed by a sweat, leucocytosis and later often an improvement of all symptoms. Gay of the University of California, has used the non-toxic remnant of the typhoid bacillus, sensitized with typhoid immune serum, injected intravenously in typhoid patients. The reaction to this typhoid vaccine has aroused the phenomena named with hyperleucocytosis. The series of patients treated have apparently done better than when managed without intravenous vaccination. Dr. Gay will have the opportunity this summer to give this form of treatment a thorough trial with suitable hospital control. If it may be done, I hope he will also treat a second group of typhoid patients with a non-bac-

terial protein and a third group without vaccination, that the result in the three groups may be compared. The subject of the therapeutic use of vaccines should have the coöperative study of the clinician and immunologist if we may expect to solve the problem. Commercial stock vaccines, as used so generally, are a disgrace to the medical profession. The fault lies with the doctors, not with the manufacturers. The latter supply the demand and one may not blame them because they increase the demand by a ridiculous literature. Subcutaneous vaccination may be harmless, nevertheless the use of any remedy which is not rational is demoralizing to the profession and to the sick. I condemn the practice and, although the statement is strong, I think it is justified by its abuse to-day.

Dr. Rufus I. Cole (New York): I shall confine my attention to the discussion of the application of the principles of immunity (which we have heard to-day so well presented) to one disease, namely acute lobar pneumonia.

First, I should like to make a few remarks concerning vaccine treatment. It seems especially appropriate that we should have had this discussion concerning vaccine treatment to-day, since it is just ten years ago that Sir Almeroth Wright came to this country to present a series of lectures on vaccine therapy, and immediately following this visit the application of this form of therapy became widespread. It is of interest to consider what explanation there may be for the errors that may have been made in the unlimited application of this method of treatment. When we consider the scientific foundation on which this method was based, we find that only those applications which were founded on definite experimental evidence have stood the test of time. Prophylactic vaccination, that is vaccination of the uninfected person, had a well-established experimental basis. For the production of immunity to bacteria by vaccination in the animal or man after infection had already occurred, there was no definite experimental proof. Even to-day almost the only experimental evidence indicating the possibility of a rapid production of immunity by vaccination in the infected animal is furnished by the work of Gay and of Jobling, concerning which Dr. Hektoen has spoken. These observations are of great interest. It has long been evident that there is more in immunity than the changes observed in the blood. This is shown by the facts that in natural immunity there may be no discoverable alteration of the blood, and

that active immunity is much more effective than any brought about by the transference of serum or blood from the immunized to the uninfected animal. The attempts to discover the non-humoral factors in immunity may throw great light on questions concerning specific therapy. It seems to me, however, that as clinicians, engaged in the treatment of human patients, we should go slowly in the application of these newly discovered principles. We are justified in carrying out new methods of specific treatment only when we are sure of doing no harm, and when we are sure that we are proceeding according to well-established principles. It is true that the value of these new immunizing methods must finally depend on the results of their application in patients, and it is justifiable that well-trained observers should carry on these therapeutic tests, but it seems wrong for the general practitioner to use these methods under conditions in which he can draw no valid conclusions. From my own experiments, as well as a study of the literature, I believe that there is no justification for vaccine therapy in acute lobar pneumonia, except the very recent experiments which have been mentioned. I have tried by various methods to produce very rapid immunization of animals and have not been able to produce enough immunity to be of any possible therapeutic value within six or seven days.

Nevertheless, it is questionable whether we should condemn indiscriminately all forms of vaccine therapy and should discourage further efforts to find an experimental justification. I know of very few patients, even those with chronic infections, in whom high grades of immunity have been produced by vaccination. In inducing immunity in horses for the production of serum, much greater care and attention to detail have been observed than has been customary in the attempts to immunize patients.

In regard to serum therapy, on the other hand, there is good experimental justification for testing its clinical value in pneumonia. The facts which justify this investigation are as follows: Animals may be rendered highly resistant to pneumococci by the previous injection of living or dead organisms. By transferring the blood or serum of these animals to normal animals, the latter may also be rendered resistant to infection. Finally, by transferring the blood or serum of the actively immunized animals to animals which have already been infected, the latter may be cured, provided that the infection is not too great, that the serum treatment be not too

long delayed, and finally that the type of organism employed for causing the infection be the same as that used in immunizing the animal supplying the serum.

The questions to be settled by clinical study are whether or not the serum can be obtained of sufficient strength and be administered in sufficient amount and sufficiently early to influence the course of the disease, and finally whether the results obtained are sufficient to justify a general application of the method.

Dr. Park has discussed so fully the method of clinical application of this form of therapy that I shall not go into the matter further. I must take issue with him, however, in regard to one point, namely, his advice that every patient seriously ill of pneumonia should receive a preliminary injection of serum of Type I, before the type of infecting organism is determined. While I realize that we are unusually favorably situated at the Rockefeller Institute, there should be no difficulty in every good hospital in the country in differentiating the type of organism in practically all cases, within 8 to 24 hours of the patient's admission to the hospital. It is probably not advisable that this method of treatment should be at once applied in rural districts where facilities for accurate study are not obtainable. The greatest danger is not that an occasional case will be treated too late, but that the serum will be administered indiscriminately without ever determining the type of pneumococcus concerned and thereby judgment as to the value of the serum will be rendered impossible. Since mistakes have been made with vaccine therapy, we should proceed with caution in the introduction of serum therapy and should try to carry out the method with full attention to all details.

I believe that the use of immune serum in cases due to infection with Type I pneumococcus is efficacious. This opinion is based on a relatively small clinical experience, but in addition to the clinical results, which have been excellent, the opinion is based on two observations, first, that the bacteria have very quickly disappeared from the blood after the administration of serum, and second, that following the administration of serum immune bodies appear in the blood, just as they do after natural recovery. This latter fact does not prove that recovery depends entirely upon the appearance of such immune bodies in the blood; there are undoubtedly other factors concerned. But by supplying this factor it is very probable that we may change the course of the disease.

Acute lobar pneumonia will cause 6,000 deaths in New York City this year. When we realize that 2,000 of these will be due to pneumococcus Type I alone, more than all the deaths due to typhoid fever, scarlet fever, and all forms of meningitis combined, it is evident that this one type is important enough to give it independent consideration. We should regard the different forms of pneumonia, due to different types of pneumococci, as distinct entities, just as we do typhoid fever and paratyphoid infections.

Dr. Theodore C. Janeway (Baltimore): There are four points which I should like to make in regard to this illuminating discussion. The first is that progress comes by conflict and not by agreement and that we need both the enthusiast and the critic for the correct solution of a problem. We need both the man from Minnesota and the man from Missouri. I trust that we shall all carry away scientific stimulus and illumination from the admirable discussions of this complex subject and that we shall also carry away from this meeting a picture, the picture of a man who, after a number of years of diligent work on this problem,—years in which he has published results which have seemed favorable to vaccine therapy,—stands up and tells us without hesitation that there is nothing in his work of great importance as compared with the older methods of treatment. This is the ideal practitioner, who combines enthusiasm and criticism. When we hear a man criticise his own work fearlessly we are all ready to listen to him. If we gain positive advances from the debauch of vaccine therapy, out of which the country is now beginning to emerge, as I believe we shall, through stimulation of investigation, we must admit that the psalmist was right when he said "Surely the wrath of man shall serve thee."

A second important point is that whatever conclusions we introduce into our premises in the consideration of a subject we shall draw out of again, but we shall obtain nothing of scientific value with them. If you cultivate from the tonsils or teeth of patients suffering from an obscure disease a particular organism and with that organism make a vaccine, and after treatment with this vaccine note improvement in your patient, and from this conclude that you have demonstrated the cause of that obscure lesion, you are not going to advance the science of medicine. You may have some reason to believe that the organism stands in relation to the lesion, but the relationship is not proven by such an experiment. You can-

not prove the cause by the cure and the cure by the cause at the same time. An autogenous vaccine is not a vaccine obtained from anywhere in the same patient, but only from the lesion itself or the circulating blood. I am not going into the discussion of the question of focal infection, but I say that if you draw such conclusions as to the relationship of the focus and the remote lesion, you are putting conclusions into the premises of your argument and taking them out again.

The matter of specificity in vaccine and serum therapy is a very complex one. If we are to use specific vaccines and sera with the idea that the specificity is important, we must not rely on a mere cultural specificity, but have immunological identity. That seems particularly important in relation to some newer types of sera which have real promise against organisms which do not produce true toxins. If, as Dr. Cole has said, we are to get results from serum therapy in pneumonia, it will be by the use of truly specific sera. When we turn to the question of intravenous injection of vaccine, for the cure of such diseases as typhoid, we are confronted by a reaction which can be produced by other substances non-bacterial in nature, such as proteose, and even salt solution. Blood transfusion from a donor of the proper group may be followed by a similar reaction. In one interesting case we had recently, a transfusion was done for hæmorrhage in typhoid fever and was followed by an immediate chill, high fever, and then a critical defervescence which lasted for three days. I believe this reaction is similar to the reaction still occasionally observed after salvarsan, and formerly so common when the water was not freshly distilled. I believe further that the most severe reaction is apt to be followed by the greatest benefit. We are dealing here with very complex processes in which a specific factor may enchance the non-specific one. Before we can safely apply these new facts, the men who are working on these problems must have time and opportunity to elucidate them. They may afford us safe means for the treatment of some acute and chronic diseases, but that is for the future. The process is not unattended with danger and very unfavorable results have been known to follow such intravenous injection; to my personal knowledge several deaths.

There is one other point. If there is anything with which I reproach myself in looking back over my treatment of cases of acute sepsis with pyogenic organisms in the blood, it is my occasional

failure to make a thorough search for the primary focus of metastatic foci of suppuration. The man who has found an organism in the blood is apt either to make a fatal prognosis, or to consider that he has found a weapon with which to combat the infection by means of vaccine. I repeat that the first duty of every physician in patients with sepsis is to make a thorough and painstaking search for the primary focus of infection and for all accessible secondary foci, to continue to search for such foci, and to evacuate surgically each one that he finds.

Dr. Thomas Wood Hastings (New York): After the papers of the afternoon and the discussion which have preceded, it will not take long to call attention to a few points which are worth while referring to in specific therapy. The first essential factor is to determine the specific cause of infection. Specific therapy, especially in the form of vaccine therapy, has been miserably abused, because care has not been taken to determine the specific factor involved. The necessity for the determination of the causative agent is as important with sera as with vaccines. For years the same error has been made in the employment of serum-therapy, and this has brought discredit upon sera. That a specific bacteriological diagnosis must be made before one can hope to use successfully sera or vaccines is particularly true in regard to streptococcus infection.

It is known as the result of recent work with streptococcus viridans, and also with pneumococcus, that different strains may be isolated from various foci of the infected body, or from the blood in septicaemia. The streptococci fall into two distinct main groups,—(A) streptococcus viridans; (B) streptococcus pyogenes; and these groups may be subdivided into several types; and the types again into strains. From studies by Thro* it would seem that the subdivision of types into individual strains is unnecessary and cannot rightfully be maintained biologically, but it is just as important to determine the group and type of the individual strain, as it is to distinguish between two different organisms, for instance, cocci and bacilli. As Dr. Park has suggested, this fact may be the reason for the failure of the anti-streptococcus serum. The more recent

* J. Infect. Dis., Vol. XV. No. 1., July, 1914, pp. 234-243.
J. Infect. Dis., Vol. XVII. No. 1., July, 1915, pp. 227-233.

discoveries would lead to the belief that the use of polyvalent sera is just as reckless and as little desirable as the use of polyvalent vaccines (polyvalent here being used in its primary sense, and not as an equivalent for the term "mixed vaccine").

Dr. Billings has laid stress upon the autogenous vaccine regardless of the organism found. It is known that for prophylactic antityphoid inoculations certain stock strains of relatively low "toxicity" are best for immunization. For the gonococcus also, it is known (Torrey) that certain few strains may be proven better than the majority for therapeutic immunization and that these may be only slightly "toxic." The same theory of selection is true for streptococcus viridans, in that most strains are practically non-toxic and possess to a small degree immunizing power and fixability by complement, so that certain strains which possess both the latter properties in more than the usual degree (to be determined by inoculation of animals) should give results more assuring than an autogenous strain. And, lastly, for the pneumococcus vaccine a selected strain of the prevailing less toxic type causing infection, and certainly not the autogenous strains when of the more toxic type, should be used.

For streptococcus infections of the chronic form a satisfactory serum is not available, according to the experience of observers who have used sera, and there are no satisfactory results with sera recorded for acute streptococcus infection. No one, from the literature alone, may justly conclude that the appropriate bacterial vaccine does not hasten recovery from localized chronic infection (excepting localizations in bony structures), and prevent the recrudescence of recurring infections. Doubt as to the justifiability and desirability of bacterial vaccines for acute infections is in the ascendency, mainly on account of the lack of experimentally founded basis for such a procedure. Those who are familiar with the late Surgeon-General Sternberg's book on Immunity (1895) and with studies in immunity since then, will feel that the possibility of immunizing experimentally an animal with living bacteria by injection of repeatedly increasing doses, at certain intervals,—thus developing the conditions of an animal invaded by living bacteria, tolerating injections of similar living antigen,—not only justifies, but demands, the attempt to treat patients, suffering from acute infections, by means of the methods for active immunization.

Dr. Billings has mentioned particularly the employment of vaccines in the chronic arthritides, giving the impression that vaccine therapy has given no favorable results for other conditions than arthritis; and that the condition of nutrition and hygienic surroundings have an important bearing on the recovery of the patient. The latter part of the statement is trite, however, for any method of treatment (with or without vaccines or sera), and more important even than the surroundings and general hygienic condition, is the patient's nutrition. One may enhance recovery if attention is given to these factors, as is well known, and practically the same statements apply to medical and surgical procedures. No practitioner should employ vaccine therapy in patients poorly nourished or cachectic, except with the greatest caution; just as a surgeon would select with great care, and handle with reserve patients under such conditions.

Here it would be well to call attention to the statement of Dr. Billings that he has used autogenous streptococcus viridans and other organisms in mixed vaccines for arthritis and that his doses have rarely been above 500 million for streptococcus viridans. From a large experience it is safe to say that no results will be obtained with streptococcus viridans vaccines when given in maximum doses so small as 500 million, and as a rule, beginning with an initial dose of 50 to 100 million for arthritis (or any other streptococcus viridans infection) the dosage may be increased rapidly to 3 billion, 5 billion, 8 billion or even 16 billion, according to the tolerance of the patient, if an adult: for a child or an infant the dosage should be reduced in proportion.

In cases of chronic localized infection which have become systemic, and especially in septicaemia with localization, as phlebitis or periostitis, there is no question that the comparison of a large number of cases not treated by vaccine and those treated by vaccine shows that the latter method is entirely justified by results. If the patient is given opportunity to recover without interference with the properly conducted specific therapy, results are gained which will not be duplicated without specific therapy. For example, in subacute or chronic endocarditis, clinically malignant types running a relatively short course with symptoms of intense sepsis and the milder forms with intermittent febrile reactions and exacerbations in the cardiac symptoms, there is no question but that vaccine therapy

employed carefully for long periods, will give results not obtained without specific treatment.

In looking over the records of Bellevue Hospital for ten years one finds there were recorded no spontaneous recoveries from infectious endocarditis in cases in which organisms (usually streptococci) had been isolated from the blood. Since vaccines have been used for such cases during the past eight years, there have come to knowledge seven cases of recovery, resulting in a chronic cardiac valvular lesion,—a few of them in the wards of Bellevue (Thompson*), and a few of them in the hands of private physicians.

The investigations of Drs. Dochez and Cole have resulted in the important discovery of the four types of pneumococci, and if one intends to use pneumococcus serum (as Dr. Park has emphasized, and as I would emphasize in regard to vaccine) it must be borne in mind that serum for one certain prevailing type should be prepared, and that with one or two types one is dealing with organisms that liberate, by disintegration, intensely toxic products, and that such types should not be used for vaccine; it may be recalled also that the latter types will not produce protective sera when inoculated into animals. I am mentioning these facts because in certain wards of Bellevue Hospital we have used pneumococcus vaccine, for a number of years, in several series of cases, prepared from an organism which belongs to a group relatively non-toxic and having immunizing powers. The latter fact has been established by injecting into white mice and small white rats such doses that death results on the fifth or sixth day and then injecting, on the second day after such a 5-day or 6-day lethal dose, a heated vaccine prepared from the same strain of pneumococcus. Considerable reduction in mortality in the vaccinated animals has been obtained.

From the study of vaccine injection for pneumonia in certain wards of Bellevue Hospital it is evident that one cannot draw conclusions from the results of work during one or two years, but, by comparing inoculated cases with uninoculated controls from several series over periods of from five to seven years consecutively one may safely compare results and make deductions.

Uncriticisable conclusions cannot be drawn from observations on the bacteriology of the sputum in respiratory tract infections, including pneumonia, until studies have been carried through several

* Amer. J. Med. Soc., 1909, Vol. 138, p. 169.
Transact. Assoc. Amer. Physicians, 1909.

consecutive years, for the yearly variation is considerable. Yearly fluctuations in the death rate in pneumonia are so wide that several years must elapse before conclusions can be safely drawn in regard to results of vaccine therapy, and likewise serum therapy. This is true for lobar pneumonia, particularly.

Comparison of the vaccinated with the non-vaccinated cases in several series, over a period of eight years, shows that a reduction in the death rate from pneumonia may be obtained through employment of vaccines, provided that one uses for the preparation of vaccine a strain of pneumococcus which is not intensely toxic. This fact, which can be readily corroborated by the hospital records, does not change deductions from theoretical considerations. There is no question but that the desirable method for the specific treatment of pneumonia patients would be with serum injected intravenously or subcutaneously if, with any carefully selected type of antigen, a serum may be obtained which will bring about a reduction in the death rate over a period of several years. This method will then have proven a most desirable therapy.

From the work of *Elser some years ago on pneumococci, it was suggested that better results might be obtained by intravenous than by subcutaneous injection of bacterial vaccines. I do not know that this has been applied to chronic localized infections or to septicaemia. From the records of results obtained after careful diagnostic work and careful immunizing therapy in the hands of men competent to do such work, one must conclude that by subcutaneous injection of vaccine one may get results not to be obtained in other ways. Whether reports of the next few years will show that intravenous injection is much more efficacious than subcutaneous and therefore will be the chosen method, one cannot forecast.

As to the employment of bacterial vaccines by the general practitioner who is not trained for such work, he should be ashamed for being misled by manufacturers. The exploitation of vaccine therapy which has spread over the country through the advertisements and personal visits of representatives of drug firms, is most unjustifiable. Under such guidance the first essential for specific therapy with vaccines or sera is never complied with, that is, that a specific bacteriological or immunological diagnosis through testing of blood serum, must be made. There is one development in specific therapy which seems known only to those familiar with immunological work,

* Personal communication.

and that is that practical application of immunology is complicated and requires knowledge, experience and judgment. There are many capable men, especially among the younger physicians, scattered throughout the country, who have the knowledge and judgment to conduct specific therapy as it should be carried out. The investigations of the last three or four years on pneumonia, streptococcus infections, and typhoid fever, have cleared up a few points for the specialist, but have made it much more difficult for the understanding of the general practitioner, and have put it far beyond his conception. The rank and file of the profession must leave this work to the specialist who has the knowledge and equipment to carry on the work. The use of commercial vaccines should be absolutely condemned and discontinued, with few exceptions, for any purpose other than prophylaxis.

The cost mentioned by Dr. Billings of applying such methods in a properly conducted practice in a medical center, should not enter into the question at all, since it is possible to give the majority of patients requiring specific treatment the best that can be obtained in the dispensaries and laboratory clinics. At least this is the case in New York.

Dr. Frederick P. Gay (Berkeley): I have not much to add to the discussion, but since my name has been used particularly in relation to a somewhat novel method of vaccine therapy, I want to say in defence that I belong to the humoral school of immunity and have had no relation with the earlier uses of vaccine in treatment advocated by Wright. I have been convinced against my will that vaccine therapy may be of use in certain types of disease. I believe moreover in the use of sensitized or serum treated vaccines, although I had a prejudice against it before my own investigations were made. These facts may have some weight as evidence of the convincing nature of the results obtained.

In relation to what Dr. Billings said as to the value of control cases in testing any method of therapy, I think that the value of controls will appeal to anyone who has done much experimental work. There may be certain cases, however, where controls are obtained in another way. If, as in the case of vaccine treatment of typhoid fever, we could determine exactly what goes on in the respective bodies of cases that do and those that do not respond

to the treatment, it would be far more important than control cases treated by another method. In other words, more emphasis might frequently be laid on a comparative, rather than a statistical method.

Dr. William H. Park (New York): I should like to add just one word and that is that it is absurd that laboratories should send out sera without testing for potency and stating the results. Anti-streptococcus and antipneumococcus sera are sent out by all the producing plants without a word of explanation as to the potency and type of antibodies. If physicians do not insist on this explanation, the laboratories may not make the determinations, as they are quite difficult. Antimeningitis serum, for instance, if properly made, is a definite curative substance but much that has been sold is little better than normal horse serum. I believe that if nothing is known by the producer as to the potency of the serum the preparation ought to be labelled "This serum is sent out without having been tested as to its value."

As to the friendly controversy between Dr. Cole and myself as to the routine treatment of pneumonia before or after the identification of the types, I believe my point of view is justified by the fact that during the past month at the Rockefeller Institute one case of pneumonia waited for its serum injection 15 hours and died 12 hours later, and the only case of type-one infection that died at the Presbyterian Hospital, waited 24 hours for the determination and the case died as identification was completed. In the Rockefeller Institute and in the Presbyterian Hospital they have everything available for a quick identification of the type and yet even in these places such occasional delays will take place. How much more will this delay be where such facilities and skill are not available. I think it is better therefore to give three out of four severe cases an unnecessary dose of potent type-one antipneumococcus serum, rather than to omit the serum altogether in a suitable case or take the risk of waiting for the identification of the strain.

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